Critical Care

RESEARCH Open Access

Heterogeneous cardiovascular responses to acute mean arterial pressure augmentation in septic shock: the role of ventriculo-arterial coupling and venous return

Emilio Daniel Valenzuela[1*], Pablo Mercado[2], Juan Nicolás Medel[3], Vanessa Oviedo[1], Luigi Gabrielli[4], Michel Slama[5], Jan Bakker[1,6], Ricardo Castro[1] and Jaime Retamal[1]

Abstract

Background In patients with septic shock, vasopressor-induced mean arterial pressure (MAP) augmentation is commonly used to restore tissue perfusion; however, patients may exhibit divergent cardiovascular responses despite achieving similar arterial pressure targets. We hypothesized that this heterogeneity reflects the differences in ventricular adaptation to increases in arterial load and venous return determinants.

Methods We conducted a prospective physiological observational study in mechanically ventilated adults with septic shock who underwent transient MAP augmentation from approximately 65 to 85 mmHg after the initial hemodynamic resuscitation. MAP was increased by norepinephrine dose escalation or by adding vasopressin according to clinical judgment. Comprehensive transthoracic echocardiography was performed immediately before and after MAP augmentation. Patients were classified a priori according to the relative changes in cardiac output (CO): flow recruitment (> 15% increase), stable flow (− 15% to + 15%), or flow deterioration (> 15% decrease). Changes in effective arterial elastance (Ea), end-systolic elastance (Ees), VA coupling (Ea/Ees), stroke volume, left ventricular ejection fraction (LVEF), analogue mean systemic filling pressure (Pmsa), and derived venous return variables were analyzed.

Results Thirty-two patients were included. Despite comparable increases in MAP, the cardiovascular responses were heterogeneous: 10 patients (31%) exhibited flow recruitment, 17 (53%) maintained a stable flow, and 5 (16%) developed flow deterioration. Patients with flow deterioration showed a greater increase in Ea without a proportional increase in Ees, resulting in worsening VA coupling (ΔEa/Ees + 0.22 IQR [0.01–0.81]), whereas VA coupling remained stable or improved in patients with preserved or increased flow ($p = 0.035$). Flow deterioration was also associated with reduced LVEF and changes in the derived venous return indices, which may have contributed to the observed reduction in forward flow. Changes in VA coupling correlated with changes in IVCT ($\rho = 0.788$, $p < 0.0001$), MPI ($\rho = 0.599$, $p < 0.0003$), stroke volume ($\rho = -0.418$, $p = 0.017$), and LVEF ($\rho = -0.431$, $p = 0.0139$).

*Correspondence:
Emilio Daniel Valenzuela
emvalenzuelae@uc.cl

Full list of author information is available at the end of the article

© The Author(s) 2026. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

Conclusions Acute MAP augmentation elicits heterogeneous cardiovascular responses in patients with septic shock despite similar increases in arterial pressure. Flow deterioration is characterized by worsening VA coupling, reduced stroke volume, and impaired systolic adaptation, potentially modulated by changes in the derived venous return indices.

Introduction

The mean arterial pressure (MAP) remains a central target during septic shock resuscitation, and transient MAP augmentation is increasingly used as a physiological challenge to determine whether a higher perfusion pressure improves tissue perfusion [1–3]. However, the achieved arterial pressure does not fully characterize the cardiovascular response because similar increases in MAP may be accompanied by markedly different changes in forward blood flow. Indeed, acute vasopressor-induced increases in MAP may be associated with increases, minimal changes, or even reductions in cardiac output despite comparable changes in arterial pressure [4]. This dissociation is particularly relevant in septic shock, where profound vasodilation, altered venous capacitance, and variable myocardial dysfunction coexist and continuously modify the relationship between pressure and flow [5, 6]. Therefore, the cardiovascular response to acute MAP augmentation may provide physiological information that cannot be inferred from MAP alone.

The net change in cardiac output during MAP augmentation reflects the interaction among several simultaneous effects of the vasoconstriction. On the venous side, restoration of vascular tone may increase the stressed blood volume and mean systemic filling pressure, thereby favoring the pressure gradient for venous return [7]. However, vasoconstriction may simultaneously increase resistance to venous return, potentially limiting the increase in cardiac filling and flow. On the arterial side, the same intervention increases the load against which the left ventricle ejects. Therefore, maintenance of stroke volume requires adequate ventricular adaptation to this acute increase in arterial load. Consequently, the direction and magnitude of the cardiac output response should be regarded as an integrated result of changes in venous return, ventricular performance, and arterial load, rather than as a direct consequence of the increase in MAP.

Ventriculo-arterial (VA) coupling provides a useful framework for examining the arterial and ventricular components of this response. Effective arterial elastance (Ea) integrates the net arterial load imposed on the ventricle, whereas end-systolic elastance (Ees) provides an index of ventricular systolic performance; their relationship, expressed as Ea/Ees, describes the mechanical matching between the ventricle and arterial system [8, 9]. During acute MAP augmentation, stroke volume preservation requires sufficient adaptation of ventricular systolic performance to the imposed increase in arterial load. An increase in Ea that is not matched by an adequate ventricular response may result in worsening VA coupling and impaired ejection [10–12]. However, VA coupling captures only the arterial–ventricular interaction and does not account for the upstream determinants of cardiac filling. Analogue mean systemic filling pressure (Pmsa), the pressure gradient for venous return, and resistance to venous return provide complementary estimates of the venous conditions under which the ventricle operates [4, 13, 14]. The vasoactive strategy used to achieve MAP augmentation may further modulate this response because different vasopressors exert distinct effects on arterial tone, venous capacitance, and cardiac performance [11, 15]. However, the mechanisms by which these arterial, ventricular, and venous components interact to determine the cardiac output response to acute MAP augmentation in septic shock remain poorly understood.

Therefore, we hypothesized that the heterogeneous response of CO to acute MAP augmentation in septic shock reflects differences in the integrated cardiovascular adaptation to the intervention, particularly the balance between ventricular adaptation and arterial loading, which is potentially influenced by changes in venous return determinants. Our primary objective was to characterize these responses by combining comprehensive echocardiography, VA coupling, and derived indices of venous return, and to determine whether flow recruitment, stable flow, and flow deterioration were associated with distinct patterns of cardiovascular adaptation. We also examined the relationship between changes in VA coupling and the indices of ventricular mechanics. Exploratory analyses were performed to assess the baseline cardiovascular profile associated with flow deterioration and whether the response differed according to the vasopressor strategy used to achieve MAP augmentation.

Materials and methods

Study design and MAP augmentation protocol

This prospective physiological observational study included mechanically ventilated adult patients with septic shock who underwent transient mean arterial pressure (MAP) augmentation following initial hemodynamic resuscitation.

Transient MAP augmentation was performed in patients with persistent signs of hypoperfusion, operationally defined as the presence of a capillary refill time

≥ 3 s and/or an arterial lactate concentration > 2 mmol/L after initial hemodynamic resuscitation and in the absence of evidence of preload responsiveness according to a multimodal assessment of dynamic indices. Preload responsiveness was assessed using the pulse pressure variation, stroke volume variation, and inferior vena cava distensibility. Patients were considered non–preload responsive when at least two of the following criteria were absent: pulse pressure variation ≥ 13% [16], stroke volume variation ≥ 12% [17], or inferior vena cava distensibility ≥ 18% [18], assessed at a tidal volume of 8 mL/kg. MAP was increased from approximately 65 to 85 mmHg using either norepinephrine dose escalation or the addition of vasopressin at a fixed dose of 0.03 U/min, according to the treating physician's decision. Vasopressor selection was not protocolized and reflected the routine clinical practice.

The study was approved by the Human Ethics and Safety Committee of the Pontificia Universidad Católica de Chile in accordance with the Declaration of Helsinki (Protocol ID: 200318004), and written informed consent was obtained from all patients or their legally authorized representatives. Clinical trial registration: Not applicable. This was an observational physiological study without random allocation to the study intervention.

Cardiovascular assessment

Comprehensive transthoracic echocardiography was performed immediately before and after achieving the target MAP by a certified operator according to the current recommendations for advanced critical care echocardiography [19], using a Mindray M9 ultrasound system (Bio-Medical Electronics Co., Shenzhen, China).

The following variables were recorded before and after MAP augmentation: cardiac output (CO), stroke volume (SV), left ventricular ejection fraction (LVEF), heart rate (HR), central venous pressure (CVP), capillary refill time (CRT), arterial lactate concentration, and myocardial performance index (MPI).

The central venous pressure was measured at end-expiration at the base of the A wave [20].

Assessment of ventriculo-arterial coupling

Ventriculo-arterial (VA) coupling was assessed as the ratio of effective arterial elastance (Ea) to left ventricular end-systolic elastance (Ees) [8]. Effective arterial elastance, an integrative index of arterial load, was calculated as previously described by Chemla et al. [21]:

$Ea = Pes / SV;$

where Pes represents end-systolic pressure, estimated as 0.9 × systolic arterial pressure (SAP), and SV represents the stroke volume.

End-systolic elastance (Ees) was estimated noninvasively using the validated single-beat method described by Chen et al. [22], according to the following equation:

$Ees = [DBP - ENd(est) \times Pes] / [SV \times ENd(est)],$

where DBP represents diastolic blood pressure, and ENd(est) represents the estimated normalized ventricular elastance at the onset of ejection. ENd(est) was derived according to the Chen single-beat method using the left ventricular ejection fraction, arterial pressure, and normalized systolic timing. The pre-ejection period (PEP) was measured from the ECG R wave to the onset of aortic flow, whereas the left ventricular ejection time (LVET) was measured from the onset to the end of aortic flow using pulsed-wave Doppler of the left ventricular outflow tract. The total systolic period was defined as the time from the ECG R wave to the end of the aortic flow, and the normalized systolic timing (tNd) was calculated as PEP/(PEP + LVET), as previously described [11].

VA coupling was subsequently calculated as the Ea/Ees ratio, with higher values indicating greater ventriculo-arterial uncoupling.

Changes in cardiovascular variables were expressed as absolute and relative differences between baseline and post-augmentation measurements.

Assessment of venous return

Venous return physiology was assessed using the analogue mean systemic filling pressure (Pmsa), pressure gradient for venous return, and resistance to venous return. Pmsa was estimated using the Parkin mathematical model as $Pmsa = 0.96 \times CVP + 0.04 \times MAP + c \times CO$, where c is an anthropometrically derived coefficient based on age, height, and weight [13, 14]. The pressure gradient for venous return was calculated as Pmsa – CVP, and the resistance to venous return as (Pmsa – CVP)/CO. These variables were calculated at baseline and after MAP augmentation, and their changes were expressed as post-VPT minus baseline values [4].

Classification of cardiovascular responses

Patients were classified according to the relative change in cardiac output following MAP augmentation. Three cardiovascular response groups were defined a priori:

1. Flow recruitment: increase in cardiac output of > 15%.
2. Stable flow: change in cardiac output between – 15% and + 15%.
3. Flow deterioration: a decrease in cardiac output of > 15%.

A 15% change in cardiac output was selected a priori, consistent with the threshold commonly used to define a clinically meaningful hemodynamic response in

studies of fluid responsiveness [17, 23]. Although originally developed to evaluate preload responsiveness, this threshold was applied as an operational criterion to classify the magnitude and direction of the cardiovascular response to MAP augmentation and was not intended to define discrete biological phenotypes.

Statistical analysis

Continuous variables are presented as median [25th–75th percentiles], and categorical variables are presented as counts and percentages. The baseline characteristics and cardiovascular responses to MAP augmentation were compared among the three predefined flow-response groups using the Kruskal–Wallis test for continuous variables and Fisher's exact test for categorical variables. When appropriate, pairwise comparisons were performed using Dunn's post-hoc test with Bonferroni correction. Within-group comparisons between baseline and post-augmentation measurements were performed using the Wilcoxon signed-rank test.

In addition, patients with flow deterioration were compared with the pooled group of patients with preserved or increased flow using the Mann–Whitney U test for continuous variables and Fisher's exact test for categorical variables. Changes in hemodynamic, ventriculo-arterial coupling, ventricular performance, and venous return variables were calculated as post-augmentation minus baseline values, except for changes in cardiac output, which were expressed as relative percentage changes.

Associations between changes in VA coupling and changes in cardiac output, stroke volume, left ventricular ejection fraction, mitral annular systolic velocity (s'), myocardial performance index, and isovolumetric contraction time were assessed using Spearman's rank correlation coefficients.

To evaluate whether the cardiovascular response to MAP augmentation differed according to the vasopressor strategy, linear mixed-effects models with patient-level random intercepts were fitted to account for repeated measurements within individuals. The fixed effects included time (baseline versus post-augmentation), vasopressor strategy (norepinephrine dose escalation versus addition of vasopressin), and time × vasopressor strategy interaction. These models were applied to hemodynamic, venous return, arterial load, ventricular performance, and VA coupling variables.

Exploratory analyses were performed to identify the baseline cardiovascular characteristics associated with flow deterioration following MAP augmentation. Analyses were performed using the available cases for each variable, and missing data were not imputed. All statistical tests were two-sided, and a p-value < 0.05 was considered statistically significant.

Results

Study population

Thirty-two mechanically ventilated patients with fluid-resuscitated septic shock undergoing transient mean arterial pressure (MAP) augmentation were included in the study. The median APACHE II score was 20 (IQR 14–26), and pneumonia was the most frequent source of infection (63%). Baseline MAP was 65 (IQR 64–68) mmHg while patients were receiving norepinephrine (0.18 ± 0.12 $\mu g \cdot kg^{-1} \cdot min^{-1}$). Preload responsiveness indices were low, with a pulse pressure variation of 5% (IQR 4–7%), stroke volume variation of 8.5% (IQR 3.0–12.9%), and inferior vena cava distensibility of 5.6% (IQR 2.2–13.0%). MAP augmentation was achieved by norepinephrine dose escalation in 20 patients (63%) and by the addition of vasopressin (0.03 U/min) in 12 patients (37%). The baseline demographic and clinical characteristics are summarized in Table 1.

Cardiovascular responses to acute MAP augmentation

Despite comparable increases in arterial pressure, acute MAP augmentation elicits markedly heterogeneous cardiovascular responses. Based on the predefined changes in cardiac output, three response groups were identified:

Table 1 Demographic and clinical characteristics

	All $n=32$	Flow recruitment ΔCO > +15% ($n=10$)	Stable flow −15% ≤ ΔCO ≤ +15% ($n=17$)	Flow deterioration ΔCO < −15% ($n=5$)	*p* value
Age, y.o.	71 ± 9	75 ± 9	72 ± 8	65 ± 10	0.133
Sex, female (%)	16 (50)	5 (50)	9 (53)	2 (40)	0.878
APACHE II score	20 [14–26]	24 [17–27]	20 [14–26]	14 [13–21]	0.247
SOFA score at ICU admission	10 [6–12]	11 [8–12]	9 [6–17]	8 [5–11]	0.265
Duration of Mechanical Ventilation, days	7 [3–15]	7 [3–16]	7 [3–15]	7 [3–22]	0.922
ICU length of stay, days	13 [7–19]	13 [7–29]	14 [7–18]	12 [4–25]	0.910
Norepinephrine days	5 [3–13]	4 [3–10]	5 [3–15]	9 [4–23]	0.658
AVP use during VPT	12 (38)	3 (30)	5 (29)	4 (80)	0.102
ICU Mortality, n(%)	10 (31)	2 (20)	5 (29)	3 (60)	0.281

Continuous data were expressed as mean ± SD or median [25th–75th percentiles]. Categorical variables expressed as number. APACHE II = Acute Physiology and Chronic Health Evaluation; SOFA = Sequential Organ Failure Assessment; ICU = Intensive Care Unit, AVP = vasopressin; VPT = vasopressor test

flow recruitment (ΔCO > 15%; $n = 10$, 31%), stable flow (ΔCO between − 15% and + 15%; $n = 17$, 53%), and flow deterioration (ΔCO < − 15%; $n = 5$, 16%) (Table 2).

Ventriculo-arterial (VA) coupling worsened following MAP augmentation (ΔVA + 0.22 [0.01–0.81]) only in patients with flow deterioration. In contrast, VA coupling remained stable or improved in patients with stable flow (ΔVA − 0.12 [− 0.38 to + 0.09]) and flow recruitment (ΔVA − 0. 13 [− 0.47 to + 0.16]) (Table 2).

Cardiovascular adaptation according to flow response

Compared with patients with preserved or increased cardiac output, those with flow deterioration exhibited distinct patterns of cardiovascular adaptation during MAP augmentation (Table 3). They developed a significantly greater increase in effective arterial elastance (ΔEa + 0.71 [0.42–0.76] vs. +0.28 [0.17–0.47] mmHg/mL, $p = 0.008$), whereas the increase in end-systolic elastance was smaller (ΔEes + 0.26 [− 0.71 to + 0.55] vs. +0.52 [0.07–0.99] mmHg/mL, $p = 0.150$). Consequently, arterial loading increased disproportionately relative to ventricular adaptation, resulting in worsening VA coupling (ΔEa/Ees + 0.22 [0.01–0.81] vs. −0.12 [− 0.42 to + 0.09], $p = 0.035$).

Flow deterioration was also associated with altered determinants of venous return, characterized by a decrease in the pressure gradient for venous return (Δ − 0.81 [− 1.38 to + 0.61] vs. +1.17 [0.83–1.80] mmHg, $p = 0.001$) and a greater increase in resistance to venous return (Δ + 0.26 [0.17–0.38] vs. +0.10 [0.04–0.17] mmHg·min/L, $p = 0.016$), whereas changes in analogue mean systemic filling pressure were similar between groups (ΔPmsa + 0.59 [− 2.45 to + 4.22] vs. +1.87 [0.01–2.93] mmHg, $p = 0.737$).

Flow deterioration was accompanied by a reduction in stroke volume (ΔSV − 6.21 [− 10.15 to − 5.86] mL vs. +5.68 [2.34–10.43] mL, $p < 0.001$), a decrease in left ventricular ejection fraction (ΔLVEF − 13.38% [− 16.00 to − 4.14] vs. +3.41% [− 1.72 to + 8.14], $p = 0.026$), and a more pronounced decrease in heart rate (ΔHR − 11 [− 26 to − 8] bpm vs. −2 [− 4 to + 2] bpm, $p = 0.003$). IVCT increased in patients with flow deterioration (ΔIVCT + 11 [-3–24] ms vs. − 7 [− 21 to + 3] ms, $p = 0.038$), whereas changes in the myocardial performance index did not differ significantly between the groups (ΔMPI + 0.10 [− 0.07 to + 0.24] vs. − 0.06 [− 0.18 to 0], $p = 0.161$). Changes in capillary refill time and arterial lactate levels were also similar between the groups ($p = 0.418$ and $p = 0.166$, respectively).

At baseline, patients who subsequently developed flow deterioration showed a higher-flow, lower-arterial-load profile, with numerically higher cardiac output and stroke volume, lower Ea and VA coupling, higher venous return pressure gradient, and lower resistance to venous return. Although none of these differences reached statistical significance, they showed moderate effect sizes and were considered exploratory (Supplementary Table 1).

Relationship between ventriculo-arterial coupling and ventricular performance

Changes in VA coupling were significantly associated with several indices of ventricular performance. Worsening VA coupling correlated with reductions in stroke volume and LVEF, worsening MPI, and IVCT prolongation, whereas no significant associations were observed with changes in cardiac output or mitral annular systolic velocity (Fig. 1).

Exploratory analyses

Exploratory analyses were performed to identify the physiological characteristics associated with flow deterioration following MAP augmentation.

Patients with flow deterioration more frequently underwent MAP augmentation using vasopressin than norepinephrine (80% vs. 29.6%; odds ratio 9.5, Fisher's exact $p = 0.053$).

In linear mixed-effects models, significant time × vasopressor strategy interactions were observed for cardiac output (β = −816 mL/min, $p = 0.038$) and heart rate (β = −9.58 bpm, $p < 0.001$), indicating different trajectories during MAP augmentation between the two strategies. In contrast, no significant interaction was observed for the stroke volume, effective arterial elastance, end-systolic elastance, VA coupling, LVEF, MPI, or IVCT. The differential cardiac output trajectory was accompanied by a marked difference in the heart rate response, whereas the stroke volume and VA coupling responses did not differ significantly between the strategies (Supplementary Table 2).

Discussion

The principal finding of this physiological study was that similar MAP augmentation elicited markedly heterogeneous cardiovascular responses. Most patients maintained or increased their cardiac output, whereas a subset exhibited flow deterioration accompanied by worsening VA coupling, impaired systolic performance, and reduced stroke volume, potentially modulated by changes in the derived venous return indices. These findings suggest that the cardiovascular response to MAP augmentation depends not only on the increase in arterial pressure but also on the integrated interaction between arterial loading, ventricular adaptation and venous return.

Acute MAP augmentation simultaneously modifies the arterial and venous determinants of cardiovascular performance [7]. Therefore, the resulting change in cardiac output reflects the integrated response to several simultaneous changes in loading conditions. Patients with preserved or increased forward flow exhibited a more

Table 2 Cardiovascular responses to acute MAP augmentation according to changes in cardiac output

	Flow recruitment ΔCO > + 15% Baseline	Flow recruitment ΔCO > + 15% VPT	Flow recruitment ΔCO > + 15% Δ	Stable flow − 15% ≤ ΔCO ≤ + 15% Baseline	Stable flow − 15% ≤ ΔCO ≤ + 15% VPT	Stable flow − 15% ≤ ΔCO ≤ + 15% Δ	Flow deterioration ΔCO < − 15% Baseline	Flow deterioration ΔCO < − 15% VPT	Flow deterioration ΔCO < − 15% Δ	Δ *p* value
Hemodynamic variables										
MAP, mmHg	64 (64–67)	84 (83–86)	18 (18–22)	67 (64–69)	87 (84–90)	22 (15–24)	64 (64–65)	85 (85–86)	20 (19–22)	0.662
CO, mL/min	4646 (3293–5677)	5723 (3988–6884)	26 (19–29)%	5821 (5015–6428)	5819 (4877–6479)	2 (-5–6)%	7038 (6703–7862)	4422 (3615–6364)	-24 (-37–-16)% *†	**< 0.001**
Stroke volume, mL	56.30 (41.02–58.94)	70.62 (50.54–80.59)	11.43 (9.32–13.01)	63.73 (53.85–71.82)	67.66 (54.25–71.79)	2.85 (0.76–5.68)	77.84 (74.87–79.00)	71.62 (53.28–76.91)	-6.21 (-10.15–-5.86) *†	**< 0.001**
Heart rate, bpm	88 (72–103)	89 (70–110)	2 (-2–5)	94 (88–100)	93 (82–95)	-3 (-5–-1)	94 (79–101)	80 (76–83)	-11 (-26–-8)*†	**0.002**
Venous return physiology										
Pmsa, mmHg	16.46 (11.69–16.92)	17.64 (11.55–21.92)	2.16 (0.20–4.19)	16.75 (12.26–18.63)	17.09 (14.91–19.13)	1.77 (-0.48–2.91)	17.31 (13.77–20.96)	19.05 (13.04–22.31)	0.59 (-2.45–4.22)	0.865
Venous return driving pressure, mmHg	5.91 (5.46–8.46)	7.77 (6.85–10.88)	2.03 (1.26–2.42)	7.90 (6.79–8.53)	8.83 (7.49–9.59)	0.90 (0.67–1.26)	8.84 (6.55–9.66)	7.55 (6.35–9.01)	-0.81 (-1.38–0.61)*†	**< 0.001**
Resistance to venous return, mmHg·min/L^{-1}	1.43 (1.30–1.65)	1.47 (1.32–1.75)	0.04 (0.02–0.08)	1.32 (1.26–1.45)	1.49 (1.31–1.61)	0.16 (0.05–0.18)	1.19 (1.15–1.57)	1.44 (1.34–1.94)	0.26 (0.17–0.38)*	**0.002**
Arterial load and ventriculo-arterial interaction										
Ea, mmHg/mL	1.68 (1.52–2.13)	1.80 (1.59–2.40)	0.18 (0.10–0.24)	1.44 (1.34–1.65)	1.79 (1.69–2.16)	0.42 (0.27–0.52)	1.25 (1.09–1.75)	1.91 (1.56–2.51)	0.71 (0.42–0.76)*†	**< 0.001**
Ees, mmHg/mL	1.09 (0.63–2.96)	1.48 (0.78–3.28)	0.14 (-0.01–0.73)	1.47 (1.29–1.90)	2.30 (1.90–2.58)	0.59 (0.22–1.12)	1.97 (1.30–2.54)	2.31 (1.05–2.60)	0.26 (-0.71–0.55)	0.065
VA coupling, Ea/Ees	1.69 (0.73–2.32)	1.19 (0.65–2.66)	-0.13 (-0.46–0.16)	0.97 (0.64–1.18)	0.81 (0.68–1.03)	-0.12 (-0.38–0.09)	0.68 (0.63–1.04)	1.13 (0.78–1.59)	0.22 (0.01–0.81) †	0.109
Left ventricular systolic performance										
LVEF, %	57 (51–65)	62 (51–74)	2.63 (-1.20–7.17)	63 (58–68)	65 (59–70)	3.98 (-4.26–7.51)	62 (61–67)	58 (54–61)	-13.38 (-16.00–-4.14)*	0.080
IVCT, ms	65 (28–89)	63 (32–76)	-6 (-25–5)	48 (38–58)	40 (38–49)	-7 (-19–4)	41 (32–61)	55 (34–79)	11 (-3–24)	0.107
Mitral s' wave, cm/s	10.34 (7.52–14.87)	10.84 (8.11–15.23)	0.30 (-0.73–0.98)	13.00 (10.00–15.17)	12.05 (10.82–16.40)	-0.62 (-1.23–1.00)	13.05 (8.81–13.39)	11.60 (6.95–13.50)	-1.79 (-1.86–0.11)	0.404
MPI	0.68 (0.61–0.92)	0.60 (0.49–0.85)	-0.08 (-0.13–-0.03)	0.55 (0.45–0.59)	0.46 (0.40–0.55)	-0.06 (-0.18–0.05)	0.58 (0.48–0.72)	0.58 (0.51–0.68)	0.10 (-0.07–0.24)	0.308
Tissue perfusion variables										
CRT, s	3.00 (2.25–4.00)	2.50 (1.62–3.00)	-0.50 (-1.00–0.00)	2.00 (2.00–5.00)	2.00 (2.00–3.00)	0.00 (-0.50–0.00)	2.80 (2.00–8.00)	3.00 (1.50–5.00)	-0.50 (-1.00–-0.50)	0.288
Lactate, mmol/L	2.50 (2.17–3.12)	2.45 (1.85–3.73)	0.00 (-0.25–0.40)	4.20 (2.30–4.80)	3.60 (2.10–4.70)	-0.20 (-0.60–-0.10)	2.20 (2.10–4.40)	2.10 (1.60–2.70)	-0.90 (-1.20–-0.10)	0.081

Values are expressed as median (interquartile range). Patients were classified according to the relative change in cardiac output (CO) during the vasopressor test as **flow recruitment** (ΔCO > + 15%) $n = 10$, **stable flow** (− 15% ≤ ΔCO ≤ + 15%) $n = 17$, or **flow deterioration** (ΔCO < − 15%) $n = 5$. Baseline and post-intervention values are presented together with the corresponding change (Δ = VPT − baseline), except for ΔCO, which is expressed as relative percentage change. Venous-return variables were available in 29 patients (flow recruitment, $n = 9$; stable flow, $n = 16$; flow deterioration, $n = 4$). Analyses were performed using available cases without imputation. MAP, mean arterial pressure; CO, cardiac output; VPT, vasopressor test; Pmsa, analogue mean systemic filling pressure; CVP, central venous pressure; Ea, effective arterial elastance; Ees, left ventricular end-systolic elastance; VA coupling, ventriculo-arterial coupling; LVEF, left ventricular ejection fraction; IVCT, isovolumetric contraction time; MPI, myocardial performance index; CRT, capillary refill time. *$p < 0.05$ for flow deterioration (ΔCO < − 15%) versus flow recruitment (ΔCO > + 15%); †$p < 0.05$ for flow deterioration versus stable flow (− 15% ≤ ΔCO ≤ + 15%)

Table 3 Cardiovascular changes during acute MAP augmentation in patients with preserved or increased flow versus flow deterioration

	Flow recruitment / stable flow (*n* = 27) Δ	Flow deterioration (*n* = 5) Δ	Δ *p* value
Hemodynamic variables			
MAP, mmHg	21 (16–24)	20 (19–22)	1.000
CO, mL/min	7 (0–21)%	-24 (-37–-16)%	**< 0.001**
Stroke volume, mL	5.68 (2.34–10.43)	-6.21 (-10.15–-5.86)	**< 0.001**
Heart rate, bpm	-2 (-4–2)	-11 (-26–-8)	**0.003**
Venous return physiology			
Pmsa, mmHg	1.87 (0.01–2.93)	0.59 (-2.45–4.22)	0.737
Venous return driving pressure, mmHg	1.17 (0.83–1.80)	-0.81 (-1.38–0.61)	**0.001**
Resistance to venous return, mmHg·min/L	0.10 (0.04–0.17)	0.26 (0.17–0.38)	**0.016**
Arterial load and ventriculo-arterial interaction			
Ea, mmHg/mL	0.28 (0.17–0.47)	0.71 (0.42–0.76)	**0.008**
Ees, mmHg/mL	0.52 (0.07–0.99)	0.26 (-0.71–0.55)	0.150
VA coupling, Ea/Ees	-0.12 (-0.42–0.09)	0.22 (0.01–0.81)	**0.035**
Left ventricular systolic performance			
LVEF, %	3.41 (-1.72–8.14)	-13.38 (-16.00–-4.14)	**0.026**
IVCT, ms	-7 (-21–3)	11 (-3–24)	**0.038**
Mitral s' wave, cm/s	0.07 (-1.23–1.12)	-1.79 (-1.86–0.11)	0.220
MPI	-0.06 (-0.18–0.00)	0.10 (-0.07–0.24)	0.161
Tissue perfusion variables			
CRT, s	0.00 (-1.00–0.00)	-0.50 (-1.00–-0.50)	0.418
Lactate, mmol/L	-0.20 (-0.60–0.00)	-0.90 (-1.20–-0.10)	0.166

Values are expressed as median (interquartile range).Baseline and post-intervention values are presented together with the corresponding change (Δ = VPT – baseline), except for ΔCO, which is expressed as relative percentage change. For venous-return variables, data were available in 29 patients (preserved or increased flow, *n* = 25; flow deterioration, *n* = 4). These comparisons were performed using available cases without imputation. MAP, mean arterial pressure; CO, cardiac output; VPT, vasopressor test; Pmsa, analogue mean systemic filling pressure; CVP, central venous pressure; Ea, effective arterial elastance; Ees, left ventricular end-systolic elastance; VA coupling, ventriculo-arterial coupling; LVEF, left ventricular ejection fraction; IVCT, isovolumetric contraction time; MPI, myocardial performance index; CRT, capillary refill time

proportional increase in ventricular elastance relative to arterial elastance, maintaining or improving VA coupling. In contrast, patients with flow deterioration showed a greater increase in arterial elastance that was not accompanied by a proportional increase in ventricular elastance, resulting in worsened VA coupling and reduced forward flow. Flow deterioration was also associated with a lower estimated pressure gradient for venous return and a greater increase in the estimated resistance to venous return, whereas changes in Pmsa did not differ significantly between the groups. These findings are consistent with the physiological framework proposed by Sunagawa and support the concept that cardiovascular performance during acute MAP augmentation depends on the dynamic interaction between ventricular contractility and arterial load, with changes in venous return determinants potentially contributing to the final flow response [8, 10].

Importantly, patients who subsequently developed flow deterioration did not exhibit greater myocardial dysfunction at baseline. Rather, they showed a strong trend toward a higher-flow, lower-arterial-load profile, characterized by a higher baseline cardiac output and stroke volume, together with lower effective arterial elastance and VA coupling (Supplementary Table 1). One possible interpretation is that circulation operating at a relatively high flow and low arterial load may be particularly sensitive to acute vascular loading. In these patients, MAP augmentation predominantly increases arterial elastance without a commensurate ventricular response, leading to reduced stroke volume and VA uncoupling. Such an acute increase in afterload may also unmask latent systolic dysfunction that is not evident under baseline low-afterload conditions, as may occur in patients with sepsis-induced myocardial dysfunction [24]. Concurrent reductions in the pressure gradient for venous return and an increase in resistance to venous return could further limit forward flow.

Rather than representing isolated latent myocardial dysfunction or afterload intolerance, flow deterioration may reflect a broader cardiovascular response to acute vascular loading, primarily characterized by insufficient arterial–ventricular adaptation and potentially modulated by changes in venous return. These interpretations of the mechanisms remain hypothesis-generating and are schematically illustrated in Fig. 2.

In the overall cohort, changes in VA coupling were associated with indices of ventricular mechanics, most strongly with isovolumetric contraction time, followed by myocardial performance index, stroke volume, and LVEF. Because IVCT represents the interval during which the left ventricle develops pressure before the aortic valve opens, its prolongation during MAP augmentation may indicate that more time is required to overcome the increased arterial load, which is consistent with less efficient ventricular adaptation. IVCT is influenced by heart rate, loading conditions, and vasoactive therapy, and should not be interpreted as a load-independent measure of contractility [25]. Nevertheless, its association with VA coupling suggests that it may provide complementary information on the dynamic ventricular response

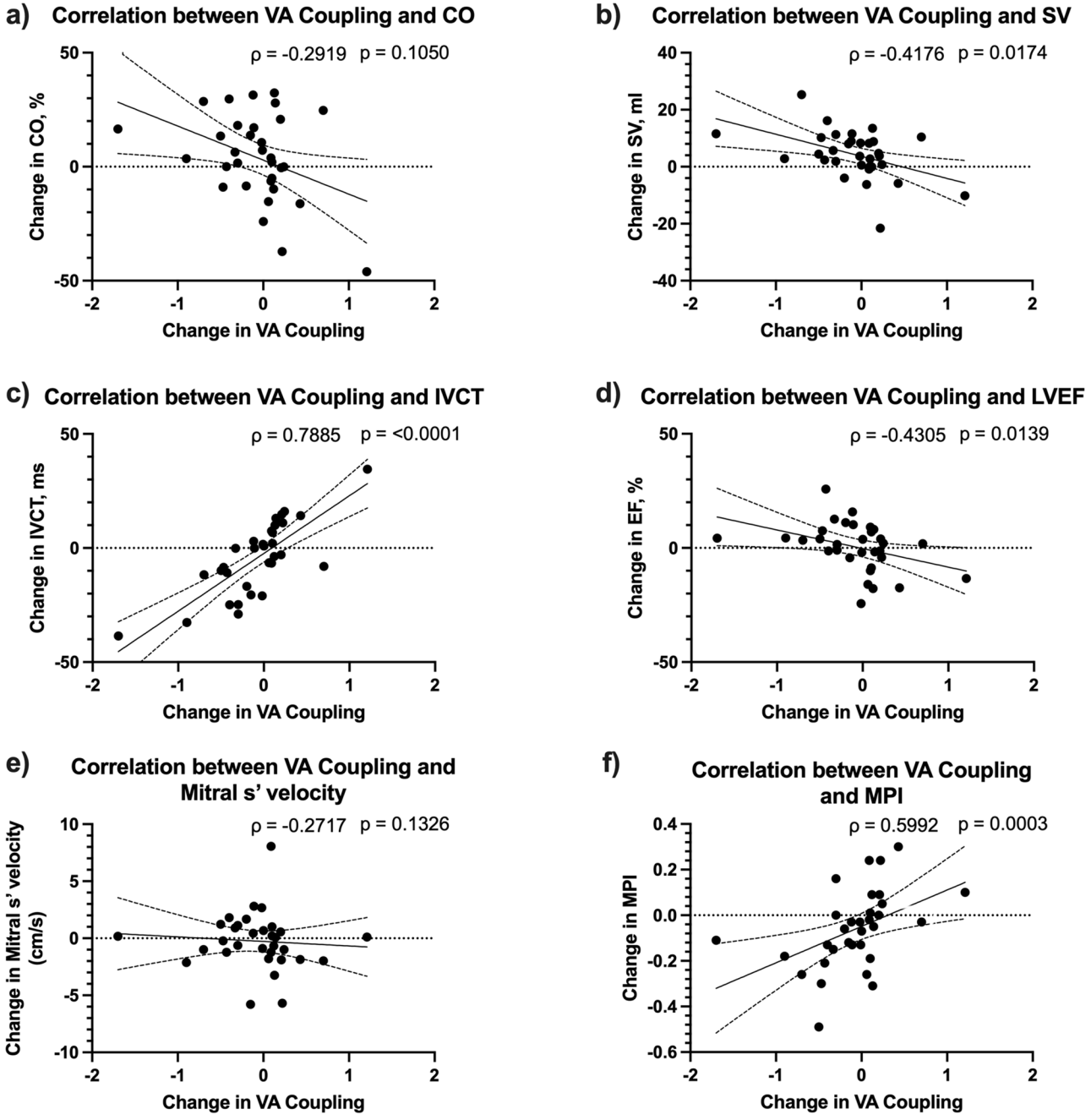


Fig. 1 Association between changes in ventriculo-arterial coupling and ventricular performance during acute MAP augmentation. Scatter plots showing the relationship between changes in ventriculo-arterial (VA) coupling and changes in cardiac output (panel **a**), stroke volume (panel **b**), isovolumetric contraction time (panel **c**), left ventricular ejection fraction (panel **d**), mitral annular s' velocity (panel **e**), and myocardial performance index (panel **f**) after acute mean arterial pressure (MAP) augmentation. Each point represents a patient. VA coupling was expressed as the ratio between effective arterial elastance and end-systolic elastance (Ea/Ees); therefore, an increase in VA coupling reflects worsening ventriculo-arterial coupling. Worsening VA coupling was significantly associated with reductions in SV and EF, prolongation of IVCT, and increase in MPI, whereas no significant association was observed with CO or mitral annular s' velocity. Solid lines represent the fitted linear regression lines, and the dashed lines represent the 95% confidence intervals. The dotted horizontal lines indicate no change from the baseline. The correlation coefficients and p-values are shown in each panel. **Abbreviations**: VA, ventriculo-arterial; MAP, mean arterial pressure; CO, cardiac output; SV, stroke volume; IVCT, isovolumetric contraction time; EF, ejection fraction; MPI, myocardial performance index; Ea, effective arterial elastance; Ees, end-systolic elastance

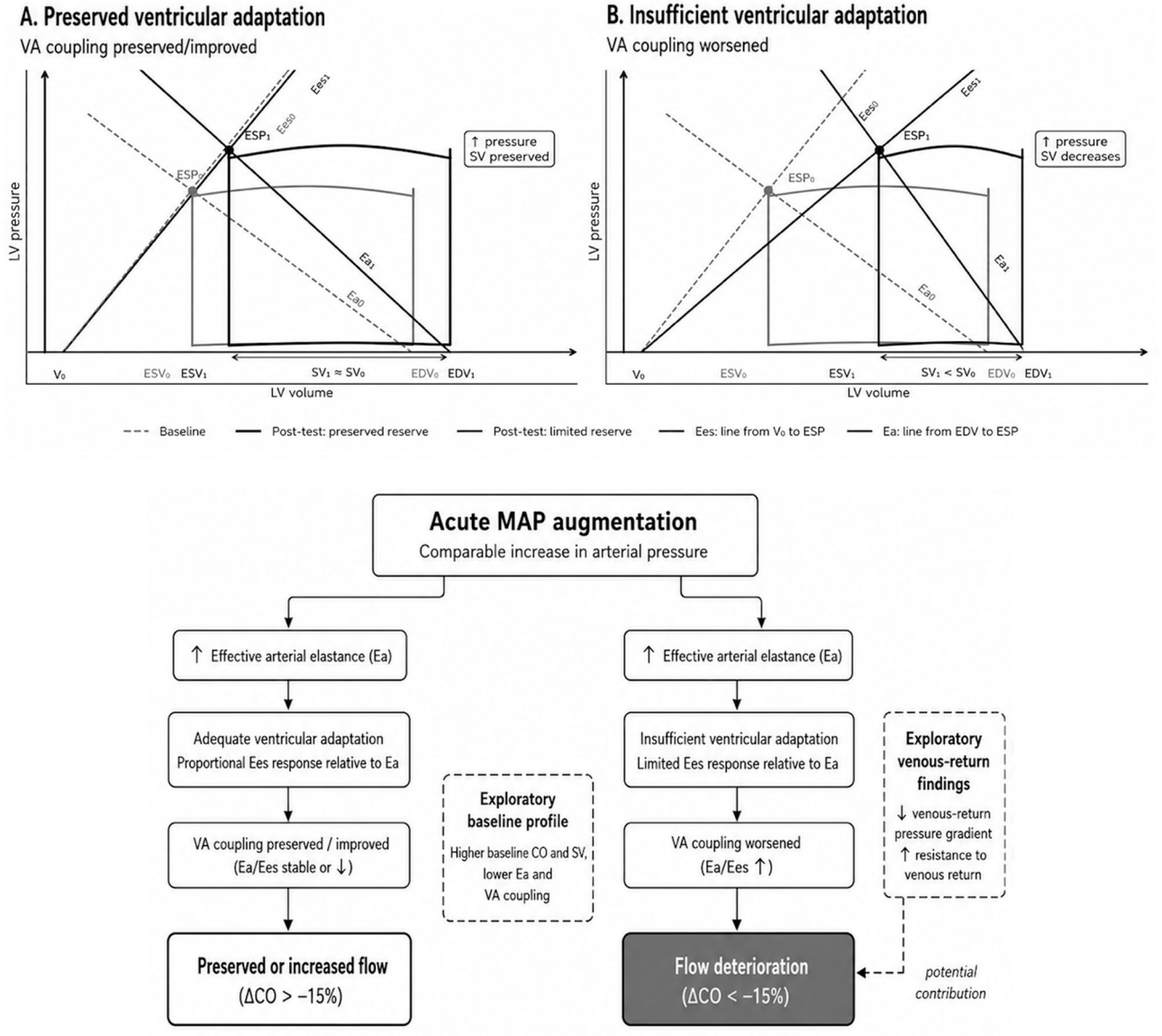


Fig. 2 Proposed physiological framework for heterogeneous cardiovascular responses to acute MAP augmentation in septic shock. Schematic representation of the proposed physiological mechanisms underlying heterogeneous cardiovascular responses to acute mean arterial pressure (MAP) augmentation in patients with septic shock. The upper panels illustrate the pressure–volume framework of ventriculo-arterial (VA) coupling during MAP augmentation. With preserved ventricular adaptation, an increase in effective arterial elastance (Ea) is accompanied by a proportional increase in end-systolic elastance (Ees), thereby preserving or improving VA coupling and maintaining or increasing forward flow. In contrast, with insufficient ventricular adaptation, an increase in Ea is not matched by a proportional increase in Ees, resulting in worsening VA coupling and reduced stroke volume The lower panel summarizes the proposed transition from MAP augmentation to the observed-flow response. Preserved ventricular adaptation is associated with preserved or improved VA coupling and maintained or increased cardiac output, whereas insufficient adaptation is associated with VA uncoupling and flow deterioration. The dashed box indicates changes in derived venous return indices, characterized by a lower estimated pressure gradient for venous return and a greater increase in estimated resistance to venous return, which may have contributed to the observed reduction in forward flow. The baseline profile of patients who subsequently developed flow deterioration was characterized by numerically higher cardiac output and stroke volume, together with lower Ea and VA coupling. The pressure–volume loops are schematic representations and were not derived from individual patient pressure–volume measurements. **Abbreviations**: CO, cardiac output; Ea, effective arterial elastance; Ees, left ventricular end-systolic elastance; EDV, end-diastolic volume; ESP, end-systolic pressure; ESV, end-systolic volume; LV, left ventricle; MAP, mean arterial pressure; RVR, resistance to venous return; SV, stroke volume; VA, ventriculo-arterial

to acute arterial load. The physiological and clinical relevance of this exploratory observation requires further prospective validation.

These findings may have implications for individualized blood pressure management in patients with septic shock. Although MAP remains a central resuscitation target [5], similar increases in MAP produce markedly different responses in cardiac output, ventricular performance, and VA coupling. Therefore, acute MAP augmentation may be viewed not only as a pressure-targeting maneuver but also as a dynamic cardiovascular stress test, revealing whether forward flow is recruited, preserved, or impaired as the vascular load increases. From this perspective, relevant physiological information may reside not only in the MAP achieved but also in how the cardiovascular system responds to that pressure is being achieved. Whether this dynamic response can help individualize MAP targets or improve clinical outcomes requires further prospective evaluation.

Changes in perfusion markers did not consistently reflect the central cardiovascular response. Despite substantial differences in forward flow, cardiac performance, and VA coupling, the changes in capillary refill time and arterial lactate levels were similar across the flow-response groups. This dissociation emphasizes that arterial pressure, forward flow, cardiac performance, and tissue perfusion represent related but non-equivalent physiological domains during short-term hemodynamic intervention. Therefore, the response to MAP augmentation should be interpreted through an integrated assessment of pressure, flow, cardiac performance, and tissue perfusion, rather than arterial pressure alone [1, 3, 6].

The vasopressor strategy may also influence the cardiovascular response to MAP augmentation. Flow deterioration occurred more frequently when MAP augmentation involved adding vasopressin to ongoing norepinephrine, although this association did not reach statistical significance, and treatment allocation was non-protocolized. Mixed-effects analyses identified different cardiac output and heart-rate trajectories according to vasopressor strategy, whereas no significant time × strategy interactions were observed for stroke volume, Ea, Ees, VA coupling, LVEF, myocardial performance index, or IVCT. Therefore, these findings do not establish a drug-specific mechanism of VA uncoupling and suggest that the cardiovascular response to acute vascular loading may be more informative than the vasopressor used to achieve it. Monitoring forward flow during MAP augmentation may help identify patients in whom achieving the intended pressure target is accompanied by a reduction in cardiac output.

This study has several limitations. First, the small sample size, particularly the limited number of patients with flow deterioration, reduced statistical power and precluded robust multivariable analyses; therefore, analyses of the baseline characteristics should be considered hypothesis-generating. Second, the change in cardiac output was used as an operational threshold to characterize the direction and magnitude of the response, rather than to define discrete biological phenotypes. Similarly, preload responsiveness was assessed using validated dynamic indices within a multimodal approach; however, values near the thresholds remain subject to a diagnostic grey zone, and the absence of preload responsiveness should not be interpreted as evidence of complete preload optimization. Third, vasopressor selection was neither randomized nor protocolized, precluding causal inference regarding differences between norepinephrine and vasopressin. Fourth, VA coupling was estimated using a noninvasive single-beat method, whereas Pmsa and venous return indices were mathematically derived rather than directly measured. Because these derived variables share measured hemodynamic components, their relationships with cardiac output should be interpreted cautiously and primarily as hypothesis-generating physiological observations. Formal patient-specific propagation of measurement uncertainty was not possible because the precision estimates for the component measurements were not prospectively collected. Finally, this was a short-term physiological study and could not determine whether the observed responses should be used to select MAP targets or improve clinical outcomes.

Conclusion

Acute MAP augmentation elicited markedly heterogeneous cardiovascular responses in patients with septic shock despite comparable increases in arterial pressure. Flow deterioration is characterized by worsening ventriculo-arterial coupling, reduced stroke volume, and insufficient systolic adaptation, potentially compounded by unfavorable changes in venous return determinants. These findings suggest that MAP augmentation may be viewed not only as a pressure-targeting intervention but also as a dynamic cardiovascular stress test, revealing the integrated ability of the circulation to adapt to acute vascular loading conditions. Whether this response can help individualize MAP targets and vasopressor therapy warrants further prospective evaluation.

Abbreviations

CCE	Critical care echocardiography
ICU	Intensive Care Unit
AVP	Vasopressin
CO	Cardiac output
SV	Stroke volume
CVP	Central venous pressure
Ea	Effective arterial elastance
LVEF	Left ventricular ejection fraction
MAP	Mean arterial pressure
Pmsa	Analogue Mean systemic filling pressure
VPT	Vasopressor test

CRT	Capillary refill time
VRdP	Venous return driving pressure
ΔSV	SV during VPT – SV basal
IVCT	Isovolumetric contraction time
Ees	Left ventricular end-systolic elastance
MPI	Myocardial performance index

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13054-026-06317-x.

Supplementary Material 1

Acknowledgements
We sincerely thank all the nurses and physicians at the participating institutions, and all the patients who contributed to this study.

Author contributions
EDV, PM, RC, JR: Contributed to the study conception and design. EDV, PM, NM and VO contributed to the clinical performance of this study. EDV, PM, NM, RC, JB, MS and JR contributed to the statistical analysis and interpretation. EDV, RC, and JR contributed to drafting this manuscript. All authors have read and agreed to the published version of the manuscript.

Funding
This work was supported by FONDECYT ANID Grants N°11201220 and FONDECYT ANID Grants N° 1241463.

Data availability
No datasets were generated or analysed during the current study.

Ethics declarations

Ethics approval and consent to participate
The study protocol was approved by the Human Ethics and Safety Committee of the Pontificia Universidad Católica de Chile (Protocol ID: 200318004) and was conducted in accordance with the Declaration of Helsinki. Written informed consent to participate was obtained from all patients or their legally authorized representatives.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Departamento de Medicina Intensiva, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile
[2]Departamento de Paciente Crítico, Facultad de Medicina Clínica Alemana, Clínica Alemana de Santiago, Universidad del Desarrollo, Santiago, Chile
[3]Unidad de Pacientes Críticos, Departamento de Medicina, Hospital Clínico Universidad de Chile, Santiago, Chile
[4]División de Enfermedades Cardiovasculares, Pontificia Universidad Católica de Chile, Santiago, Chile
[5]Medical Intensive Care Unit, CHU Sud Amiens, Amiens, France
[6]Department Intensive Care Adults, Erasmus MC University Medical Center, Rotterdam, Netherlands

Received: 19 July 2026 / Accepted: 2 September 2026

References

1. Hernandez G, Ospina-Tascon GA, Damiani LP, Estenssoro E, Dubin A, Hurtado J, et al. Effect of a Resuscitation Strategy Targeting Peripheral Perfusion Status vs Serum Lactate Levels on 28-Day Mortality Among Patients With Septic Shock: The ANDROMEDA-SHOCK Randomized Clinical Trial. JAMA. 2019;321(7):654–64. https://doi.org/10.1001/jama.2019.0071.
2. Andromeda-Shock-2 Investigators for the Andromeda Research Network SSoAR, Pain T, Latin American Intensive Care N, Hernandez G, Ospina-Tascon GA, Kattan E, et al. Personalized Hemodynamic Resuscitation Targeting Capillary Refill Time in Early Septic Shock: The ANDROMEDA-SHOCK-2 Randomized Clinical Trial. JAMA. 2025;334(22):1988. https://doi.org/10.1001/jama.2025.20402.
3. Hernandez G, Valenzuela ED, Kattan E, Castro R, Guzman C, Kraemer AE, et al. Capillary refill time response to a fluid challenge or a vasopressor test: an observational, proof-of-concept study. Ann Intensive Care. 2024;14(1):49. https://doi.org/10.1186/s13613-024-01275-5.
4. Maas JJ, Pinsky MR, de Wilde RB, de Jonge E, Jansen JR. Cardiac output response to norepinephrine in postoperative cardiac surgery patients: interpretation with venous return and cardiac function curves. Crit Care Med. 2013;41(1):143–50. https://doi.org/10.1097/CCM.0b013e318265ea64.
5. Prescott HC, Antonelli M, Alhazzani W, Moller MH, Alshamsi F, Azevedo LCP, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2026. Crit Care Med. 2026;54(4):725–812. https://doi.org/10.1097/CCM.0000000000007075.
6. Kato R, Pinsky MR. Personalizing blood pressure management in septic shock. Ann Intensive Care. 2015;5(1):41. https://doi.org/10.1186/s13613-015-0085-5.
7. Monnet X, Jabot J, Maizel J, Richard C, Teboul JL. Norepinephrine increases cardiac preload and reduces preload dependency assessed by passive leg raising in septic shock patients. Crit Care Med. 2011;39(4):689–94. https://doi.org/10.1097/CCM.0b013e318206d2a3.
8. Sunagawa K, Maughan WL, Burkhoff D, Sagawa K. Left ventricular interaction with arterial load studied in isolated canine ventricle. Am J Physiol. 1983;245(5 Pt 1):H773. https://doi.org/10.1152/ajpheart.1983.245.5.H773.
9. Monge Garcia MI, Santos A. Understanding ventriculo-arterial coupling. Ann Transl Med. 2020;8(12):795. https://doi.org/10.21037/atm.2020.04.10.
10. Kass DA, Maughan WL, Guo ZM, Kono A, Sunagawa K, Sagawa K. Comparative influence of load versus inotropic states on indexes of ventricular contractility: experimental and theoretical analysis based on pressure-volume relationships. Circulation. 1987;76(6):1422–36.
11. Guarracino F, Ferro B, Morelli A, Bertini P, Baldassarri R, Pinsky MR. Ventriculoarterial decoupling in human septic shock. Crit Care. 2014;18(2):R80. https://doi.org/10.1186/cc13842.
12. Pinsky MR, Guarracino F. How to assess ventriculoarterial coupling in sepsis. Curr Opin Crit Care. 2020;26(3):313–8. https://doi.org/10.1097/MCC.0000000000000721.
13. Parkin WG, Leaning MS. Therapeutic control of the circulation. J Clin Monit Comput. 2008;22(6):391–400. https://doi.org/10.1007/s10877-008-9147-7.
14. Maas JJ, Pinsky MR, Geerts BF, de Wilde RB, Jansen JR. Estimation of mean systemic filling pressure in postoperative cardiac surgery patients with three methods. Intensive Care Med. 2012;38(9):1452. https://doi.org/10.1007/s00134-012-2586-0.
15. Di Giantomasso D, Morimatsu H, Bellomo R, May CN. Effect of low-dose vasopressin infusion on vital organ blood flow in the conscious normal and septic sheep. Anaesth Intensive Care. 2006;34(4):427–33. https://doi.org/10.1177/0310057X0603400408.
16. Marik PE, Cavallazzi R, Vasu T, Hirani A. Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: a systematic review of the literature. Crit Care Med. 2009;37(9):2642. https://doi.org/10.1097/CCM.0b013e3181a590da.
17. Monnet X, Marik PE, Teboul JL. Prediction of fluid responsiveness: an update. Ann Intensive Care. 2016;6(1):111. https://doi.org/10.1186/s13613-016-0216-7.
18. Barbier C, Loubieres Y, Schmit C, Hayon J, Ricome JL, Jardin F, et al. Respiratory changes in inferior vena cava diameter are helpful in predicting fluid responsiveness in ventilated septic patients. Intensive Care Med. 2004;30(9):1740. https://doi.org/10.1007/s00134-004-2259-8.
19. Expert Round Table on Echocardiography in ICU. International consensus statement on training standards for advanced critical care echocardiography. Intensive Care Med. 2014;40(5):654–66. https://doi.org/10.1007/s00134-014-3228-5.
20. Magder S. Right Atrial Pressure in the Critically Ill: How to Measure, What Is the Value, What Are the Limitations? Chest. 2017;151(4):908–16. https://doi.org/10.1016/j.chest.2016.10.026.
21. Chemla D, Antony I, Lecarpentier Y, Nitenberg A. Contribution of systemic vascular resistance and total arterial compliance to effective arterial elastance

in humans. Am J Physiol Heart Circ Physiol. 2003;285(2):H614. https://doi.org/10.1152/ajpheart.00823.2002.
22. Chen CH, Fetics B, Nevo E, Rochitte CE, Chiou KR, Ding PA, et al. Noninvasive single-beat determination of left ventricular end-systolic elastance in humans. J Am Coll Cardiol. 2001;38(7):2028–34.
23. Monnet X, Shi R, Teboul JL. Prediction of fluid responsiveness. What's new? Ann Intensive Care. 2022;12(1):46. https://doi.org/10.1186/s13613-022-01022-8.
24. Repesse X, Charron C, Vieillard-Baron A. Evaluation of left ventricular systolic function revisited in septic shock. Crit Care. 2013;17(4):164. https://doi.org/10.1186/cc12755.
25. Lauboeck H. Echocardiographic study of the isovolumetric contraction time. J Biomed Eng. 1980;2(4):281. https://doi.org/10.1016/0141-5425(80)90121-1.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.