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Effects of fluid administration on arterial load in septic shock patients

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Take-home message: Fluid administration could reduce arterial load in critically patients with septic shock and acute circulatory failure. This explains why some patients increase cardiac output without increasing blood pressure.

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Abstract Purpose: To determine the effects of fluid administration on arterial load in critically ill patients with septic shock. **Methods:** Analysis of septic shock patients monitored with an oesophageal Doppler and equipped with an indwelling arterial catheter in whom a fluid challenge was performed because of the presence of systemic hypoperfusion. Measures of arterial load [systemic vascular resistance, SVR = mean arterial pressure (MAP)/cardiac output (CO); net arterial compliance, $C = \text{stroke volume (SV)}/\text{arterial pulse pressure}$; and effective arterial elastance, $E_a = 90\%$ of systolic arterial pressure/SV] were studied both before and after volume expansion (VE). **Results:** Eighty-one patients were analysed, 54 (67 %) increased their CO by at least 10 % after VE (preload responders). In the whole population, 29 patients (36 %) increased MAP by at least 10 % from preinfusion level (pressure responders). In the preload responder group, only 24 patients (44 %) were pressure responders. Fluid administration was associated with a significant decrease in E_a [from 1.68 (1.11–2.11) to 1.57

(1.08–1.99) mmHg/mL; $P = 0.0001$] and SVR [from 1035 (645–1483) to 928 (654–1452) dyn s cm⁻⁵; $P < 0.01$]. Specifically, in preload responders in whom arterial pressure did not change, VE caused a reduction in E_a from 1.74 (1.22–2.24) to 1.55 (1.24–1.86) mmHg/mL ($P < 0.0001$), affecting both resistive [SVR: from 1082 (697–1475) to 914 (624–1475) dyn s cm⁻⁵; $P < 0.0001$] and pulsatile [C : from 1.11 (0.84–1.49) to 1.18 (0.99–1.44) mL/mmHg; $P < 0.05$] components. There was no relationship between preinfusion arterial load parameters and VE-induced increase in arterial pressure. **Conclusion:** Fluid administration significantly reduced arterial load in critically patients with septic shock and acute circulatory failure, even when increasing cardiac output. This explains why some septic patients increase their cardiac output after fluid administration without improving blood pressure.

Keywords Fluid therapy · Septic shock · Arterial pressure · Cardiac output · Arterial load · Oesophageal Doppler

Abbreviations

AUC	Area under the receiver-operating characteristic curve	ESM	Electronic supplementary material	SV	Stroke volume
C	Net arterial compliance	HES	Hydroxyethyl starch	SVR	Systemic vascular resistance
CO	Cardiac output	IQR	Interquartile range	TAU	Arterial time constant
DAP	Diastolic arterial pressure	LSC	Least significant change	VE	Volume expansion
EA	Effective arterial elastance	MAP	Mean arterial pressure		
EA _{dyn}	Dynamic arterial elastance	ROC	Receiver-operating characteristic		
		SAP	Systolic arterial pressure		

Introduction

From a physiological point of view, the heart as a source of flow and pressure cannot be fully understood without taking into consideration how it interacts with the arterial system, since both the arterial vascular tree and the cardiac pump are anatomically and functionally coupled [1, 2]. In this regard, the concept of arterial load has been extensively used as a representation of net afterload opposed to the ventricular ejection, because it combines different aspects of the arterial system, such as total vascular compliance, peripheral resistance and systolic and diastolic time intervals [3, 4]. Therefore, for a given cardiac contractility, cardiovascular behaviour will be ultimately determined by the intricate interaction between the heart and the arterial vascular function, and it has been repeatedly demonstrated that maximum ventriculo-arterial efficiency is observed when cardiac performance and arterial load are optimally matched [2, 5, 6].

Persistent and profound vasoplegia is a common phenomenon associated with septic shock and, along with cardiovascular dysfunction, plays an important role in the ventriculo-arterial decoupling observed in these patients [7, 8]. Aggressive fluid resuscitation aimed at restoring adequate tissue perfusion is considered a cornerstone of the early management of sepsis and septic shock [9–11], but it is unclear what effect this therapy has on arterial load and cardiovascular efficiency.

We therefore designed this study to observe the effects of fluid administration on arterial load and its components in critically ill patients with septic shock, considering also the potential influence of concurrent vasoactive therapy, type of fluids administered and the occurrence of systemic arterial hypotension.

Methods

This is a retrospective analysis of prospectively collected data from septic shock patients admitted to the intensive care unit (ICU) of Jerez de la Frontera during May 2011 to July 2013. The study was approved by the local institutional research ethics committee and requirement of

informed consent was waived because of the retrospective study design and anonymous data management.

Patients

Patients were included in the analysis if they were diagnosed with septic shock according to the standard definition [11], received a fluid challenge during their admission in the ICU, and were monitored with an oesophageal Doppler (CardioQ or CardioQ-Combi, Deltex Medical, Chichester, UK) and an indwelling arterial catheter. Standard fluid challenge consisted of 500 mL of normal saline or synthetic colloid (Voluven 6 % hydroxyethyl starch solution 130/0.4; Fresenius Kabi, Bad Homburg, Germany), usually at an infusion rate of 500 mL during 30 min. The decision to give fluid was made by the treating physician on the basis of presumed systemic hypoperfusion. Triggers included arterial hypotension [defined as mean arterial pressure (MAP) no greater than 65 mmHg and/or systolic arterial pressure (SAP) less than 90 mmHg]; the need for vasopressor; urine output less than 0.5 ml kg⁻¹ h⁻¹ for at least 2 h; tachycardia; lactic acidosis; or delayed capillary refilling. Patients received either volume-control or pressure-control ventilation (Puritan Bennet 840, Tyco Healthcare, Mansfield, MA, USA; or Servo i, Maquet, Bridgewater, NJ, USA). No changes in ventilatory settings or the level of inotropic support were performed during the fluid challenge period.

Arterial load assessment

Our assessment of arterial load is based on a simple two-element Windkessel model [12] that comprises a resistive element: the total systemic vascular resistance [SVR = MAP/cardiac output (CO) × 80]; and a pulsatile component: the net arterial compliance [C = stroke volume (SV)/arterial pulse pressure]. Effective arterial elastance [Ea = end-systolic pressure (Pes)/SV] was used as an integrative parameter of arterial load that incorporates both steady and pulsatile components [2, 6, 13–15]. Ninety per cent of SAP was used as a surrogate of Pes in

the main analysis [14, 16], although we also calculate E_a using MAP value as an P_{es} estimate, since mean pressure drop across central aorta to radial artery is considered relatively small and constant [14, 17, 18]. The arterial time constant (τ) was calculated as the product of SVR and C . τ expresses how fast an elastic reservoir is emptied. Consequently, the higher the arterial time constant, the longer the time required for the blood flow to reach the peripheral arterial bed.

Statistical analysis

The normality of data distribution was assessed by the D'Agostino–Pearson test. The results are expressed as the median (25th–75th interquartile) or mean \pm standard deviation, as appropriate. Patients were classified according to CO and MAP increase after volume expansion (VE), as preload responders (CO increase at least 10 %) and pressure responders (MAP increase at least 10 %), respectively. These cut-offs were selected on the basis of least significant change for oesophageal Doppler CO measurements [19] and assuming an optimal arterial pressure–flow coupling. So, for a 10 % increase in CO, a 10 % increase in MAP should be expected [4, 15, 20]. Differences between groups at baseline were assessed by the Mann–Whitney U test or by means of an independent sample t test, and in their evolution over time by an ANOVA test (after logarithmic transformation of data for non-normally distributed data), followed by a Wilcoxon test or a t test with adjustment for repeated measurements. Comparison between categorical variables was assessed by a Chi-square test. The relation between variables was analysed by linear regression analysis. The ability of arterial pressure to track directional changes in CO or SV after VE was tested using a concordance analysis. Concordance was defined as the percentage of data in which the direction of change was in agreement. The area under the receiver-operating characteristic (ROC) curves was calculated to assess the performance of SVR, C , E_a and preinfusion MAP to predict a MAP increase of at least 10% after VE.

A P value less than 0.05 was considered statistically significant. All statistical analyses were two-tailed and performed using MedCalc Statistical Software version 14.1.0 (MedCalc Software bvba, Ostend, Belgium; <http://www.medcalc.org>; 2014).

Results

A total of 81 patients were included. Their characteristics and demographic data are listed in Table 1. Fifty-eight (72 %) received vasopressor support with norepinephrine, with a median dosage of 0.16 (0.09–0.31) $\mu\text{g kg}^{-1} \text{min}^{-1}$.

Table 1 Characteristics and demographics data of study population

Age (years)	65 (53–74)
Gender (M/F)	45/36
Weight (kg)	78 (70–86)
Height (cm)	167 (160–175)
ICU mortality rate, n (%)	25 (31 %)
Arterial catheter site (radial/femoral)	73/8
Vasoactives at inclusion time, n ; dosage ($\mu\text{g kg}^{-1} \text{min}^{-1}$)	
Norepinephrine	57; 0.16 (0.09–0.27)
Dobutamine	15; 6 \pm 4
Analgesia and sedative drugs	
Fentanyl, n ; dosage ($\mu\text{g kg}^{-1} \text{h}^{-1}$)	60; 1.35 (1.03–1.71)
Remifentanyl, n ; dosage ($\mu\text{g kg}^{-1} \text{min}^{-1}$)	20; 0.14 \pm 0.05
Midazolam, n ; dosage ($\text{mg kg}^{-1} \text{h}^{-1}$)	63; 0.09 \pm 0.03
Propofol, n ; dosage ($\text{mg kg}^{-1} \text{min}^{-1}$)	3; 0.9 (0.6–0.1)
Morphine, n ; dosage ($\text{mg kg}^{-1} \text{min}^{-1}$)	1; 1.80
Ventilator settings	
Tidal volume, mL/kg predicted body weight	8 \pm 1
Respiratory rate, breaths/min	20 (18–20)
Total PEEP, cmH_2O	8 (6–10)
FiO_2 (%)	70 (50–80)
Source of sepsis, n	
Abdominal	43
Pulmonary	24
Urological	8
Neurological	5
Endocarditis	1

Values are expressed as mean \pm standard deviation, median (25th–75th percentile) or absolute numbers, as appropriate

F female, FiO_2 inspired oxygen fraction, ICU intensive care unit, M male, $PEEP$ positive end-expiratory pressure, SaO_2 arterial oxygen saturation

In eight patients (10 %) the arterial blood pressure was monitored from a femoral arterial catheter (CK-0418 Arterial Catheterization Set 18 Ga, Arrow International, Reading, PA, USA). In the remaining patients, arterial pressure was measured from the radial artery (Arterial Leader-Cath 3Fr, Vygon, Ècouen, France). The source of septic shock was most commonly the abdomen. In 23 patients (28 %) volume challenge was performed using a hydroxyethyl starch (HES) solution.

Haemodynamic changes after fluid administration are summarized in Table 2. Fifty-four patients (67 %) were preload responders and 29 (36 %) increased MAP by at least 10 % from preinfusion level (pressure responders). When considering only preload responders, only 24 (44 %) were pressure responders. In these patients, pre-infusion MAP values were similar to the pressure non-responder group [74 (58–78) mmHg vs. 73 (64–84) mmHg; $P = 0.31$]. The increase in MAP after VE was 6 % (2–14 %) in the overall group and 9 % (1–18 %) in preload responders.

Effects of fluid administration on arterial load

Overall, fluid infusion decreased E_a from 1.68 (1.11–2.11) to 1.57 (1.08–1.99) mmHg/mL ($P = 0.0001$), SVR from 1035 (645–1483) to 928 (654–1452) dyn s cm^{-5}

($P < 0.01$), and tau from 0.86 (0.66–1.19) to 0.85 (0.67–1.10) s ($P < 0.05$). Net arterial compliance did not change after VE.

At baseline, arterial load was similar among preload responders and non-responders (Table 3). However, in the preload responder group, VE decreased Ea by $9 \pm 11\%$, SVR by $9 \pm 11\%$ (0–16%) and Tau by 7% (1–14%) (Table 3).

When accounting only for preload responders, no differences in preinfusion arterial load parameters between pressure responders and pressure non-responders were observed (Table 4). In preload responders in whom VE did not increase arterial pressure, fluid administration induced a significant reduction in arterial load (Ea decrease $14 \pm 9\%$), which comprised both resistive (R decrease $15 \pm 8\%$) and pulsatile components (C increase $10 \pm 16\%$) (Table 4). In preload responders with a positive pressure response, only a decrease in C was observed. In both pressure responders and non-responders, VE led to a similar reduction in arterial time constant (Table 4).

The effects of VE in preload non-responders are described in the Electronic Supplementary Material (ESM) file, Table 1. Pressure responsiveness was observed in five

of these patients (19%). When MAP was used as a surrogate of Pes in Ea calculation, the results obtained were similar (ESM file, Table 2).

Effect of presence of arterial hypotension

Overall, there are 27 hypotensive patients (33%), 18 of them in the preload responder group. Hypotensive patients had a lower Ea [1.29 (1.01–1.69) mmHg/mL vs. 1.81 (1.34–2.37) mmHg/mL; $P < 0.05$] and SVR [731 (541–1051) dyn s cm⁻⁵ vs. 1151 (748–1678) dyn s cm⁻⁵; $P < 0.01$], although they showed a similar reduction in all components of arterial load when compared with patients without arterial hypotension.

In the hypotensive preload responders in whom arterial pressure did not increase after VE ($n = 9$), Ea decreased by $12 \pm 7\%$ [from 1.22 (1.08–1.62) mmHg/mL to 1.24 (0.90–1.38) mmHg/mL; $P < 0.01$] and SVR by $11 \pm 6\%$ [from 730 (491–1008) to 655 (433–951)] dyn s cm⁻⁵; $P < 0.01$].

The presence of preload and pressure responsiveness was similar between hypotensive and non-hypotensive

Table 2 Effects of volume expansion in haemodynamic parameters according to cardiac output increase after volume expansion

	Before volume expansion	After volume expansion	<i>P</i> value ^a
CO, L/min			
Preload responders	5.5 (4.3–8)	6.3 (4.8–9.1)***	<0.001
Preload non-responders	5.7 (4.1–8.8)	6 (4.1–8.7)	
HR, beats/min			
Preload responders	98 (88–119)	94 (84–114)***	0.957
Preload non-responders	98 (76–109)	94 (72–110)*	
SV, mL			
Preload responders	53 (45–79)	63 (56–96)***	<0.001
Preload non-responders	62 (46–81)	70 (51–84)*	
CPO, W			
Preload responders	0.89 (0.67–1.24)	1.07 (0.91–1.53)***	<0.001
Preload non-responders	0.94 (0.67–1.19)	1.01 (0.70–1.25)*	
MAP, mmHg			
Preload responders	74 (60–80)	78 (65–90)***	0.025
Preload non-responders	69 (64–81)	72 (67–80)**	
SAP, mmHg			
Preload responders	106 (98–124)	119 (104–143)***	<0.001
Preload non-responders	106 (90–116)	109 (95–120)**	
DAP, mmHg			
Preload responders	54 (46–64)	56 (47–69)**	0.56
Preload non-responders	54 (44–62)	58 (46–64)**	
PP, mmHg			
Preload responders	51 (41–67)	61 (49–79)***	<0.001
Preload non-responders	43 (38–63)	49 (37–65)*	

Data are expressed as the median (25th–75th percentile). Preload responders = cardiac output increase at least 10% after fluid administration

CO cardiac output, CPO cardiac power output (mean arterial pressure \times cardiac output/451), DAP diastolic arterial pressure, HR heart rate, MAP mean arterial pressure, PP arterial pulse pressure (systolic minus diastolic pressure), SAP systolic arterial pressure, SV stroke volume

* $P < 0.05$, ** $P \leq 0.001$, *** $P \leq 0.0001$ vs before volume expansion

^a *P* value refers to group-interaction in repeated ANOVA analysis (after logarithmic transformation)

Table 3 Overall effects of volume expansion on arterial load parameters according to cardiac output increase after volume expansion

	Before volume expansion	After volume expansion	<i>P</i> value ^a
Ea, mmHg/mL			
Preload responders	1.74 (1.14–2.17)	1.60 (1.09–2.03)***	<0.001
Preload non-responders	1.35 (1.01–1.92)	1.37 (1.03–1.88)	
<i>C</i> , mL/mmHg			
Preload responders	1.16 (0.830–1.40) [†]	1.14 (0.89–1.37)	0.411
Preload non-responders	1.41 (1.05–1.86)	1.39 (0.94–1.73)	
SVR, dyn s cm ⁻⁵			
Preload responders	1058 (672–1475)	951 (652–1418)***	<0.001
Preload non-responders	949 (614–1456)	928 (656–1650)	
Tau, s			
Preload responders	0.84 (0.65–1.04)	0.83 (0.67–1.03)**	0.001
Preload non-responders	0.90 (0.70–1.49)	0.97 (0.69–1.48)	

Data are expressed as the median (25th–75th percentile). Preload responders = cardiac output increase at least 10 % after fluid administration

C net arterial compliance, *Ea* effective arterial elastance, *SVR* total systemic vascular resistance, *Tau* arterial time constant

* $P < 0.05$, ** $P < 0.001$, *** $P < 0.0001$ vs before volume expansion

[†] $P = 0.05$ vs preload non-responders

^a P value refers to group-interaction in repeated ANOVA analysis (after logarithmic transformation)

patients (67 vs. 67 %; $P = 0.80$, and 41 vs. 33 %; $P = 0.68$, respectively).

Effect of type of fluids: normal saline vs HES

Arterial load changes after fluid administration were similar between HES and normal saline groups (ESM file, Table 3). The proportion of preload and pressure responders after fluid administration was also similar between the two groups (65 vs. 67 %, $P = 0.93$; and 30 vs. 38 %; $P = 0.71$, respectively).

Effect of presence of norepinephrine therapy

Maintaining arterial pressure with vasopressor support was associated with a lower preinfusion compliance and arterial time constant. However, the presence of vasoactive therapy did not affect further arterial load response (ESM file, Table 4).

Arterial pressure changes as a surrogate for flow changes during fluid administration, and prediction of arterial pressure changes

Overall, the relationship and concordance between flow and arterial pressure changes after VE were poor (Fig. 1 and ESM file, Fig. 1). None of arterial load parameters nor preinfusion MAP level predicted the subsequent MAP increase after VE, even when considering only preload responders or the presence of arterial hypotension (ESM file, Figs. 2, 3).

Discussion

Our study shows that fluid administration can affect arterial load in critically ill patients with septic shock and acute circulatory failure. The impact of fluid therapy on arterial load seems to be associated with preload responsiveness, and changes in arterial load determined the arterial pressure response to volume expansion. However, assessment of arterial load by static measures, such as SVR, *C* or *Ea*, did not help to predict subsequent changes in arterial pressure. Moreover, the arterial load response to volume expansion was independent of concurrent norepinephrine therapy, the preinfusion arterial pressure level, or the type of fluid administered.

Arterial load represents the net opposing forces that impede ventricular ejection and comprises different aspects of the arterial system, such as arterial resistance, compliance, and arterial wave reflections [21]. Along with ventricular performance, arterial load modulates the arterial pressure and aortic blood flow waveform pattern [2]. Therefore, arterial pressure should be considered as the intricate interface between the heart pump and the arterial system [4]. However, calculation of arterial load could lead to confusion when trying to understand changes over time: mathematically, arterial load is calculated from arterial pressure and blood flow values; but, from a physiological point of view, blood flow and arterial load are actually the independent variables that determine arterial pressure. Therefore, our results should be interpreted with this in mind, and changes in arterial load observed in our study should not be considered as a spurious mathematical coupling effect.

Recently, Guarracino et al. [7] demonstrated that arterial load is generally decreased in septic shock

Table 4 Changes in arterial load parameters in preload responders categorized according to their mean arterial pressure increase

	Before fluid expansion	After fluid expansion	<i>P</i> value ^a
<i>Ea</i> , mmHg/mL			
Pressure responders	1.76 (1.09–2.12)	1.64 (1.09–2.05)	<0.001
Pressure non-responders	1.74 (1.22–2.24)	1.55 (1.24–1.86)***	
<i>C</i> , mL/mmHg			
Pressure responders	1.24 (0.77–1.39)	1.12 (0.76–1.31)*	0.002
Pressure non-responders	1.11 (0.84–1.49)	1.18 (0.99–1.44)*	
SVR, dyn s cm ⁻⁵			
Pressure responders	1021 (631–1584)	1045 (661–1589)	<0.001
Pressure non-responders	1082 (697–1475)	914 (624–1337)***	
<i>Tau</i> , s			
Pressure responders	0.84 (0.65–1.25)	0.85 (0.65–1.09)*	0.762
Pressure non-responders	0.84 (0.65–1)	0.82 (0.67–0.94)**	

Data are expressed as the median (25th–75th percentile). Preload responders = CO increase at least 10 % after fluid administration. Pressure responders = mean arterial pressure increase at least 10 % after fluid administration

Ea effective arterial elastance, *C* net arterial compliance, *SVR* systemic vascular resistance, *Tau* arterial time constant

* *P* < 0.05, ** *P* < 0.01, *** *P* < 0.0001 vs before volume expansion

^a *P* value refers to group interaction in repeated ANOVA analysis (after logarithmic transformation)

patients, irrespective of cardiac function level. The reduced arterial load could have contributed to the ventriculo-arterial uncoupling and decreased cardiovascular efficiency observed in those patients. Importantly, all these patients were previously resuscitated with fluids according to the Surviving Sepsis Campaign guidelines prior to inclusion in the study, but still remained hypotensive. So, we can hypothesize that the use of fluid therapy aimed to optimize cardiac preload could potentially contribute to impaired arterial load and ventriculo-arterial decoupling. Moreover, previous experimental studies also suggested that the typical haemodynamic profile of distributive shock (low SVR and high CO), often observed in patients with septic shock, could actually be induced by fluid administration, transforming the initial non-resuscitated hypodynamic profile into a hyperdynamic state [22, 23]. Fluid responsiveness is defined as the ability of the heart to significantly increase cardiac output in response to volume expansion. So patients can be responders with or without a concomitant increase in blood pressure. If the clinical outcome effect of fluid administration is better with both arterial pressure and flow increase or only with flow increase is not known. Although our results were not designed to confirm this hypothesis, they emphasize the vasoactive-like effect of fluid therapy in this pathological condition, and the impact on cardiovascular efficiency when no improvement in arterial pressure is seen. Furthermore, if clinicians give fluids to improve both flow and pressure, the clinical benefit of the relatively small increase in MAP observed in preload responders (from 74 to 78 mmHg) should lead one to reconsider aggressive fluid resuscitation when trying to restore organ perfusion pressure in septic patients. Indeed, while we did not record this in our study, it is possible that aggressive fluid resuscitation may

actually decrease perfusion pressure by increasing central venous pressure more than MAP.

Volume expansion triggers an intricate process involving not only venous system, cardiac function and the arterial system, but also a complex neuro-hormonal and reflex response [24]. Even though this study was not designed to determine the underlying causes, fluid-induced reduction in arterial load may have resulted from several mechanisms. Firstly, baroreflex-mediated vasoconstriction in response to hypovolaemia could be blunted by intravascular volume administration in preload responders. In practice, the interpretation is that even if flow increases, the arterial pressure rise is minimal because the vasoplegic state may have reset the cardiovascular system to maintain a lower blood pressure compared to a non-shock state. So, when flow is augmented with fluid administration, a decreased in arterial load occurs as a compensatory mechanism to maintain arterial pressure at the same level. While it is possible, it is unlikely that this physiological phenomenon was the only explanation, since the reduction in heart rate after fluid infusion (as a result of a baroreceptor-induced decreased sympathetic activity) was similar in the preload non-responder group.

Secondly, acute changes in blood flow have been demonstrated to lead to a reduction of arterial tone via flow-mediated vascular relaxation [25]. This short-term mechanism of arterial adaptation seems to be modulated by increased nitric oxide production and endothelial shear stress stimulus during fluid loading [26, 27]. Thirdly, recruitment of previously closed vessels increases the effective diameter of arterial system and, consequently, reduces arterial resistance [28].

Lastly, reciprocal changes in SVR with CO increases observed in preload responders could not accurately

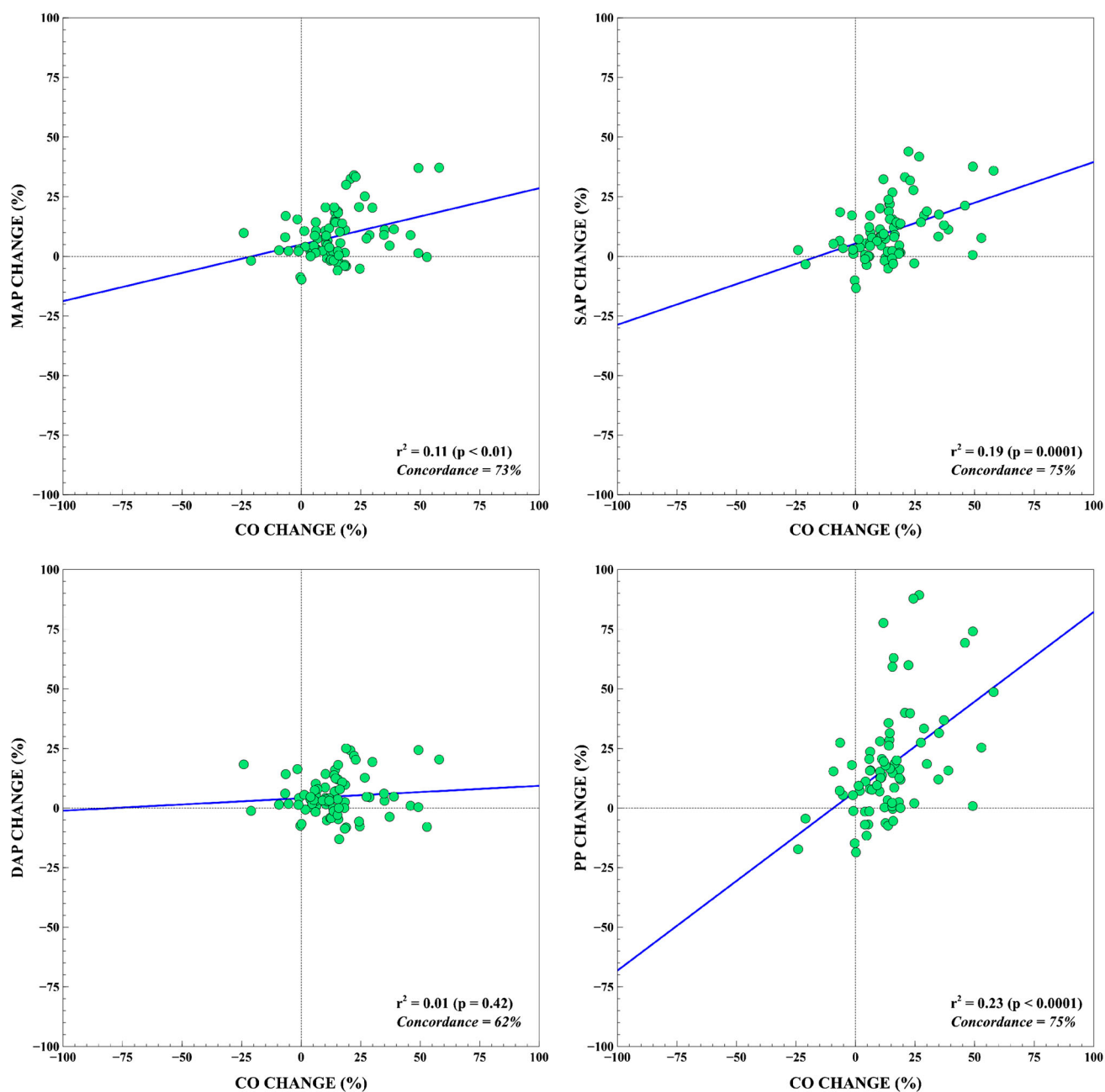


Fig. 1 Relationship and concordance analysis between cardiac output and arterial pressure changes after volume administration in septic shock patients. *CO* cardiac output, *DAP* diastolic arterial

pressure, *MAP* mean arterial pressure, *PP* arterial pulse pressure, *SYS* systolic arterial pressure. *Concordance* percentage of data in which the direction of change agreed

represent changes in arterial resistance, since we did not consider the actual critical closing pressure of the arterial system in our SVR calculation [29, 30]. However, this particular issue should not affect *C* and *Ea* estimations.

This study also confirmed that changes in arterial pressure are weakly related to changes in blood flow as a result of volume administration, in critically ill patients, and therefore should not be used as a surrogate for

tracking changes in cardiac output or stroke volume [31–33].

Interestingly, arterial load changes induced by fluid therapy have been previously demonstrated to adversely affect the reliability of haemodynamic monitoring tools utilizing pulse-contour analysis [19]. Therefore, in practice, caution should be taken when no changes in cardiac output are observed, since associated arterial load

decrease after VE could potentially mask the effects on cardiac output when measured by these techniques.

Furthermore, we also observed that none of the studied arterial load parameters predicted the arterial pressure response to fluid administration. This finding is in agreement with previous reports in which steady assessment of arterial load—as measured by Ea, C and SVR—failed to predict the blood pressure response to fluid loading [34–36]. In this regard, functional assessment of arterial load has been shown to characterize the dynamic interaction between pressure and flow, and to help to define pressure responsiveness to fluids [34, 36].

Our study has some important limitations. Firstly, the estimation of CO and flow-derived parameters was performed using an oesophageal Doppler. Because this monitoring system assumes a constant proportion of CO through the descending thoracic aorta and a fixed aortic diameter, changes in the distribution of blood flow and variations in aortic diameter due to arterial pressure changes could potentially have affected our results [37]. Secondly, the impact of positive pressure ventilation on intrathoracic pressure could influence inter-individual measurements of arterial load given differences in aortic transmural pressures [38]. However this factor should not have influenced the changes in arterial load, since no modification in ventilatory settings was performed during the fluid challenge period. Thirdly, our arterial load assessment is based on a simple two-element Windkessel model [12] and an integrative simplification, defined by the effective arterial elastance [2, 14]. A more precise and complete characterization of the arterial input impedance requires a frequency-domain analysis of the arterial pressure–flow relationship [25]. However, the technology required for this analysis is cumbersome and still far from being available in routine haemodynamic monitoring. Furthermore, Ea was calculated using radial systolic arterial pressure. Although this approach has been demonstrated to provide a reasonably good estimation of

Pes [14, 16], septic patients may exhibit a central-to-peripheral vascular tone decoupling [18], which may compromise the reliability of this calculation. However, even when using MAP as a substitute of Pes [14], our results are consistent with a significant reduction in arterial load after VE.

Finally, although we found arterial load to be significantly influenced by fluid administration, we did not evaluate the clinical consequences of this. Arterial load is an essential component of ventriculo-arterial efficiency [3, 4] and a key determinant of arterial blood pressure [2]. Therefore, increasing blood flow without a subsequent improvement in arterial pressure decreases the energetic efficiency of the heart pump as a source of pressure, since the efficiency of the cardiovascular system is considered optimal when all the pulsating energy of the left ventricle is transferred to the systemic circulation, i.e. when cardiac power is maximized [4, 15].

Conclusions

Fluid administration significantly reduced arterial load in critically patients with septic shock and acute circulatory failure. This explains why some septic patients increase their cardiac output after fluid administration without improving blood pressure.

Conflicts of interests MIMG is consultant for Edwards Lifesciences and received travel expenses from Deltex. AGC has received Honoraria from Edwards Lifesciences. AR has received Honoraria and is on the advisory board for LiDCO, Honoraria for Covidien, Edwards Lifesciences and Cheetah. MC in the last 5 years has received honoraria and/or travel expenses from Edwards Lifesciences, LiDCO, Cheetah, Bmeye, Masimo and Deltex. PGG, MGR, CO and RMG have no conflict of interest to declare.

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