Dynamic arterial elastance assessment by the pressure recording analy ical method in children with septic shock

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Abstract

***Introduction*: Septic shock in children can lead to cardiac dysfunction, leading to increased tissue hypoperfusion and mortality. Arterial elastance is a metric that denotes an arterial vessel's capacity to elevate arterial pressure and afterload through enhanced flow and rigidity. Dynamic arterial elastance (Eadyn) is regarded as a functional evaluation of arterial tone.**

***Objective*: Investigating Eadyn by the pressure recording analytical method (PRAM) and the correlation between Eadyn and other hemodynamic parameters in children with septic shock.**

***Methods*: An observational cohort study at the Pediatric Intensive Care Unit (PICU), which included children aged 6 months to 18 years with septic shock, body weight >7.5 kg, and no congenital heart disease. Eadyn and other hemodynamic variables (arterial blood pressure, central venous pressure, heart rate, cardiac output, stroke volume, and systemic vascular resistance) were measured using PRAM connected to arterial lines. All patients received initial hemodynamic resuscitation and vasoactive drugs.**

***Results*: Children with septic shock were prospectively analyzed; 8 survived, and 19 died during PICU treatment. From data analysis, we found that Eadyn correlated with cardiac index and systemic vascular resistance on the second and third days of observation, as well as with cardiac power output and stroke volume index across all three days of observation. Eadyn was also higher in the group that survived, with an area under the curve (AUC) of 78% for predicting death, according to the receiver operating characteristic (ROC) analysis.**

***Conclusion*: The evaluation of Eadyn constituted a key element in the assessment of cardiovascular function and could be useful in predicting mortality in children with septic shock.**

Keywords: Septic shock, dynamic arterial elastance, mortality.

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Introduction

Assessment of cardiac function is crucial for determining interventions and therapies aimed at optimizing hemodynamic performance in children with septic shock. (1) In septic shock, cardiac dysfunction often arises from impaired cardiac output, leading to increased tissue hypoperfusion and mortality. (2,3) Restoring blood pressure is still the main goal in most resuscitation protocols. (1,4) However, because blood pressure is influenced by the interaction between the arterial system and cardiac output, monitoring patients' response to fluid therapy can be challenging. (5,6) Consequently, even when a patient shows an increase in cardiac output from fluids and vasopressors, predicting the response in the arterial system is complicated. (7) To assess whether fluid administration will enhance the arterial system, it is crucial to evaluate both the patient's pre-

load dependency and their arterial load, which refers to stroke volume (SV) and arterial pressure. (8)
Arterial elastance (Ea) is a parameter that describes the capacity to raise arterial pressure and afterload through enhanced flow and arterial stiffness. Dynamic arterial elastance (Eadyn) is considered a functional assessment of arterial tone. Eadyn could predict arterial pressure increases following volume expansion (VE) in hypotensive patients. (7) Eadyn serves as a dynamic measure of arterial tone, can also facilitate a practical approach to managing vasoactive therapy. (9)
However, research on the hemodynamic implications of Eadyn in children with septic shock remains limited. This study aimed to investigate arterial pressure as measured by Eadyn, explore its correlation with other hemodynamic parameters, and also assess its potential as a mortality predictor in children with septic shock.

Method

Data collection
We performed a prospective observational cohort study in the Pediatric Intensive Care Unit (PICU) at Dr. Soetomo General Hospital, Surabaya, Indonesia, from August 2020 to December 2021. The study included children aged 6 months to 18 years with septic shock and body weight >7.5 kg. Children with congenital heart disease were excluded.
The patient's parents had to sign the informed consent after the researchers provided an explanation of the significance of this study. The Ethics Committee of the Faculty of Medicine at Universitas Airlangga - Dr. Soetomo General Hospital approved this study.
The data collection included patients' names, ages, genders, vital signs, and principal diagnoses. All subjects received initial therapies, hemodynamic resuscitation, and organ support therapy. Hemodynamic monitoring was performed utilizing the pressure recording analytical method (PRAM) via the Mostcare system linked to arterial lines over a three-day assessment period.

Data analysis
We performed descriptive statistics of Eadyn and other hemodynamic variables, including mean arterial pressure (MAP), cardiac index, cardiac power output (CPO), ratio of ventricular pressure (dP/dt), stroke volume index (SVI), and systemic vascular resistance index (SVRI). We computed means, medians, standard deviations, ranges, and interquartile ranges for every variable. We analyzed correlations between Eadyn and other hemodynamic variables using Spearman's correlation examination. Differences in the continuous variables between groups were tested with the Mann-Whitney U test. We also analyzed correlations between Eadyn and mortality. A significance level of 0.05 was used for all statistical tests.

Result

We conducted a prospective analysis of 27 children with septic shock at Soetomo Hospital from September 2020 to December 2021. Patients, whose hemodynamics were monitored via PRAM, were included; 8 patients survived, while 19 did not survive following medical care in the PICU. All patients underwent fluid resuscitation and administration of vasoactive agents.
The baseline characteristics of the subjects in this study were presented based on the basic characteristics of sex, age, length of stay, body weight, body height, and hemodynamic parameters over a three-day observation period. The basic characteristics of the groups are written in **Table 1**. Of the 27 subjects, 12 (44.4%) were male, while the remaining 15 (55.5%) were female. The comparison between septic shock survivors and non-survivors showed a statistically significant difference in MAP (82.79±8.93 vs. 61.06±24.78 mmHg, $p<0.05$) and Eadyn (4.99 (1.09–7.22) vs. 2.03 [0.30–9.26] mmHg/ml, $p<0.05$) on the third day of observation.
Table 2 shows the correlations between Eadyn and other hemodynamic parameters. Based on Spearman's correlation analysis and the Mann-Whitney U test, Eadyn showed correlations with cardiac index and systemic vascular resistance (SVR) on the second and third days of observation, as well as with CPO and SVI over the three-day observation period. Eadyn was found to be higher in the survivor group (**Figure 1**). The highest mean of Eadyn in a survivor group was 4.42±3.04 mmHg/ml on the first examination, but the lowest of Eadyn in the non-survivor group was 2.01 (0.43–9.97) mmHg/ml (**Table 1**). Receiver operating characteristic (ROC) analysis showed that Eadyn had an area under the curve (AUC) of 76.4% (95% CI 0.56–0.99, $p<0.05$) for predicting mortality on the third day of examination (**Figure 2**, **Table 3**). We identified Eadyn 72 hours of 3.16 mmHg/ml as the appropriate point to predict mortality (**Figure 3**).

Discussion

Children with septic shock often experience cardiac dysfunction due to reduced cardiac power, which reflects the heart's ability to pump blood effectively. Cardiac power (CP) depends on both cardiac output (blood ejected by the heart) and MAP. (10) Hypoperfusion can lead to global cellular hypoxia, contributing to high morbidity and mortality. Current guidelines for septic shock management emphasize the need for markers that can identify global tissue hypoxia as a target for resuscitation. (11) However, optimal perfusion is determined by arterial load, which depends not only on cardiac power but also on its interaction with arterial pressure. While arterial load is commonly defined by the relationship between MAP and flow (e.g., SVR), this approach neglects the cyclical aspects of blood pressure and flow produced by cardiac contractions. (12) A more thorough definition of arterial load can be captured by aortic input impedance. (9) Sunagawa et al. were among the first to propose that aortic impedance could be integrated into a single variable known as Ea. (13) This measure reflects key features of the arterial system characteristics, including compliance, resistance, and impedance. (9) Some studies continue to use Ea to characterize arterial load, incorporating factors such as SV, diastolic time constant, and systolic-diastolic periods. However, measuring these variables clinically can be challenging. To address this, Kelly et al. suggested calculating Ea using the pulmonary artery systolic and SV ratio (PAS/SV). (14) Nevertheless, a study by Segers et al. noted that different combinations of arterial compliance and right ventricular diastolic function could yield the same Ea value. (15) An alternative measure, Eadyn, is defined as the ratio of aortic pulse pressure variation (PPV) to SV variation (SVV) during the respiratory cycle, providing insight into the relationship between changes in pulse pressure and SV. (16) Some studies have shown that Eadyn, as an indicator of arterial load, can be clinically relevant. Zanon et al. found that high basal Ea predicted responsiveness to cardiac resynchronization therapy in terms of end-systolic volume. (17) Our study supported these findings, demonstrating correlations between Eadyn and SVR, SV, cardiac index, and CPO.

In this study, we demonstrated that Eadyn, measured with the minimally invasive PRAM, accurately reflected cardiovascular function in children with septic shock, as it correlated with various hemodynamic variables. Beyond evaluating cardiovascular status, Eadyn could help guide therapy in critically ill patients. It has been explored as a predictor of MAP increase following a fluid challenge and has been assessed in contexts like shock, surgery, and critical care. (18) Based on functional hemodynamics, Eadyn shows how arterial pressure can increase with fluid administration. (19,20) If Eadyn is elevated and the patient is preload-dependent, arterial pressure will rise with cardiac output (CO) after VE. In contrast, if Eadyn is low, VE may not enhance blood pressure despite fluid responsiveness, indicating a need to consider vasopressors to manage hypotension. (7,19) Guinot et al. found that using a hemodynamic algorithm incorporating Eadyn resulted in shorter norepinephrine treatment durations and reduced intensive care unit stays in patients with vasoplegic syndrome after cardiac surgery. (18) Their study also showed that a norepinephrine weaning strategy based on Eadyn reduced norepinephrine use and the incidence of acute kidney injury in post-cardiac surgery patients. (21)

In critically ill patients, maintaining stable perfusion pressure is crucial for effective cardiovascular function. Arterial pressure, as indicated by Eadyn, can reflect arterial hypotension in septic shock, signaling acute cardiovascular dysfunction, tissue hypoperfusion, worsening organ failure, and increased mortality. (22,23) Our study supported this, showing higher Eadyn values in survivors. ROC analysis confirmed Eadyn as a reliable predictor of mortality, with an AUC of 78%.

This study has limitations. Hemodynamic variables alone cannot universally predict mortality. In resuscitation, the focus should be not only on restoring perfusion but also on ensuring adequate oxygen delivery for cellular metabolism, which is influenced by the immune system, neurohormonal factors, and baroreflex function. Therefore, larger interventional studies combining Eadyn with other variables, such as biomarkers, are needed. Additionally, peripheral monitoring has limitations in assessing cardiac function in children, and vascular properties may vary with age and change rapidly during illness.

Conclusion

The evaluation of Eadyn with PRAM constitutes a key element in the assessment of cardiovascular function and can be useful in predicting mortality in children with septic shock.

Ethical consideration

The Declaration of Helsinki was followed in the conduct of this investigation. We received ethical clearance from the Faculty of Medicine, Universitas Airlangga (ethical clearance number 0166/105/3/VIII/2020).

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Disclosure

The authors report no conflicts of interest in this work.

Table 1. Subjects' characteristics

Characteristics	Survivors (n=8)	Non-survivors (n=19)	p
Age (months), median (min-max)	19.50 (12–168)	84 (9–204)	0.116[2]
Gender, n - Male - Female	 5 3	 7 12	0.398[3]
Length of hospital stay (days), median (min-max)	11 (5–65)	8 (3–55)	0.539[2]
Body weight (kg), mean±SD	22.88±16.02	23.88±12.73	0.864[1]
Body length (cm), median (min-max)	87.50 (75–153)	122 (60–160)	0.441[2]
Heart rate (beats/minute), mean±SD	128.50±25.11	105.21±35.06	0.102[1]
Respiratory rate (/minute), mean±SD	38.75±9.75	31.42±9.32	0.077[1]
Systole blood pressure (mmHg), mean±SD	90.13±12.94	78.89±21.26	0.180[1]
Diastolic blood pressure (mmHg), mean±SD	51.13±11.54	43.16±20.62	0.318[1]
Body temperature (°C), median (min-max)	37.05 (36.7–38.5)	37.5 (36.7–40.9)	0.629[2]
Eadyn 24h (mmHg/ml), median (min-max)	4.17 (0.75–10.72)	2.01 (0.43–9.97)	0.124[2]
Eadyn 48h (mmHg/ml), median (min-max)	3.48 (1.31–8.02)	1.67(0.39–10.71)	0.360[2]
Eadyn 72h (mmHg/ml), median (min-max)	4.99 (1.09–7.22)	2.03 (0.30–9.26)	0.035[2]
MAP 24h (mmHg), mean±SD	64±9.39	55.17±19.9	0.221[1]
MAP 48h (mmHg), median (min-max)	71.67 (57.33–110.67)	65.33 (29–102.33)	0.381[2]
MAP 72h (mmHg), mean±SD	82.79±8.93	61.06±24.78	0.018[1]
CI 24h (l/min/m²), median (min-max)	3.40 (1.80–4.70)	2.30 (1.40–13.60)	0.084[2]
CI 48h (l/min/m²), mean±SD	3.48±0.60	4.25±2.19	0.337[1]
CI 72h (l/min/m²), mean±SD	3.84±0.69	3.63±1.66	0.745[1]
CP 24h (Watt), median (min-max)	-0.01 (-1.17–0.09)	-0.03 (-1.91–0.62)	0.426[2]
CP 48h (Watt), median (min-max)	-0.03 (-1–0)	-0.06 (-1–1)	0.936[2]
CP 72h (Watt), median (min-max)	-0.29 (-0.82–0.2)	0.00 (-1.19–0.20)	0.287[2]
dP/dt 24h (mmHg/msec), mean±SD	0.95±0.39	0.87±0.42	0.684[1]
dP/dt 48h (mmHg/msec), mean±SD	1.02±0.23	0.97±0.39	0.731[1]
dP/dt 72h (mmHg/msec), median (min-max)	0.99 (1–2)	0.70 (0–3)	0.094[2]
SVI 24h (ml/m²), median (min-max)	24.50 (15.00–49.00)	29 (12–81)	0.632[2]
SVI 48h (ml/m²), median (min-max)	25 (21–50)	40 (9–61.54)	0.300[2]
SVI 72h (ml/m²), mean±SD	33.50±11.14	38.70±17.94	0.604[1]
SVRI 24h (dyne.sec/cm⁵/m²), median (min-max)	2227 (1098–3725)	1941 (913–8904)	0.791[2]
SVRI 48h (dyne.sec/cm⁵/m²), median (min-max)	1540 (1219–5384)	1224.5 (243–4556)	0.137[2]
SVRI 72h (dyne.sec/cm⁵/m²), median (min-max)	1481 (1216–2832)	1211(177–2731)	0.05[2]

Legend: SD=standard deviation; Eadyn=dynamic arterial elastance; MAP=mean arterial pressure; CI=cardiac index; CP=cardiac power; dP/dt=ratio of ventricular pressure; SVI=stroke volume index; SVRI=systemic vascular resistance index.

[1]Independent sample T-test; [2]Mann-Whitney test; [3]Fisher's exact test.

Table 2. Correlation between dynamic arterial elastance and other hemodynamic parameters

Hemodynamic parameters	Correlation with Eadyn	
	r value	p value
MAP		
- 24 h	0.16	0.43
- 48 h	0.05	0.82
- 72 h	0.10	0.61
Cardiac index		
- 24 h	-0.28	0.17
- 48 h	-0.56	0.00
- 72 h	-0.47	0.01
CPO		
- 24 h	-0.46	0.02
- 48 h	-0.69	0.00
- 72 h	-0.39	0.05
dP/dt		
- 24 h	-0.05	0.82
- 48 h	-0.03	0.90
- 72 h	0.08	0.68
SVI		
- 24 h	-0.73	0.00
- 48 h	-0.41	0.04
- 72 h	-0.69	0.00
SVRI		
- 24 h	0.23	0.25
- 48 h	0.55	0.00
- 72 h	0.57	0.00

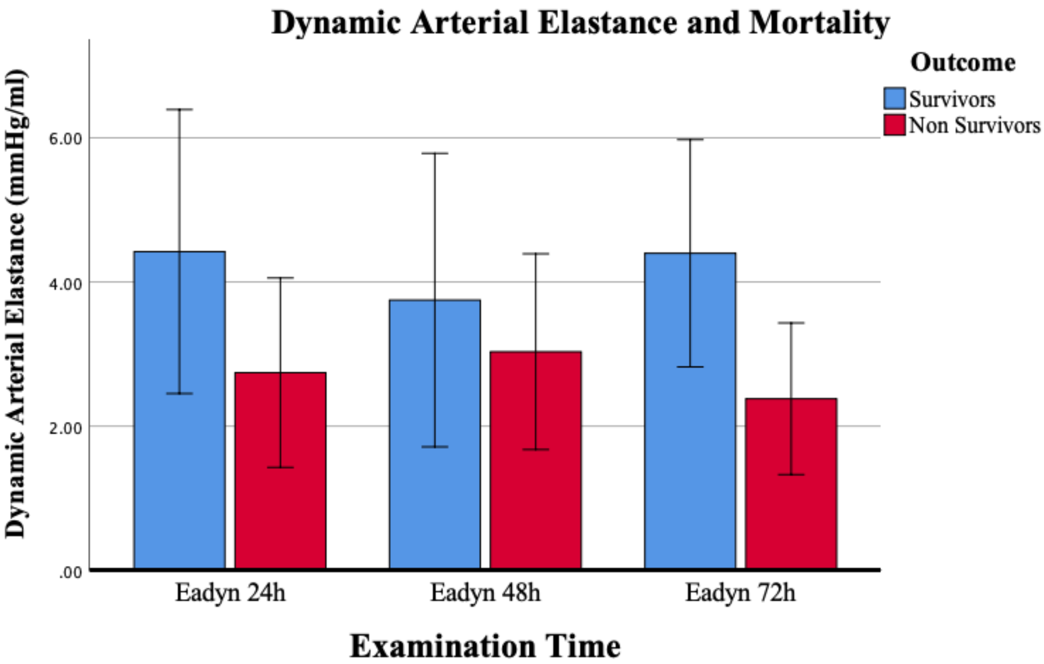
Legend: Eadyn=dynamic arterial elastance; MAP=mean arterial pressure; CPO=cardiac power output; dP/dt=ratio of ventricular pressure; SVI=stroke volume index; SVRI=systemic vascular resistance index.

Table 3. ROC analysis for dynamic arterial elastance in predicting mortality in septic shock

Test result variables	Area	SE	Asymp. sig.	Asymptotic 95% CI	
				Lower bound	Upper bound
Eadyn 24 hours	0.722	.108	0.075	.510	.934
Eadyn 48 hours	0.642	.113	0.255	.420	.864
Eadyn 72 hours	0.764	.115	0.035	.539	.989

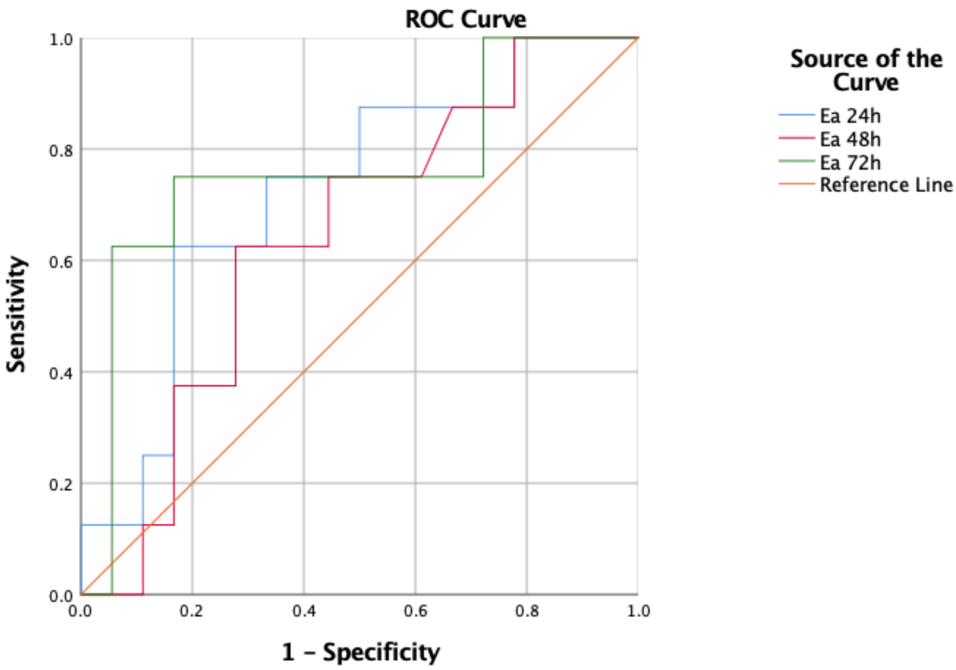
Legend: ROC=receiver operating characteristic; SE=standard error; Asymp. Sig.=asymptotic significance; CI=confidence interval.

Figure 1. Dynamic arterial elastance in the survivor and non-survivor groups



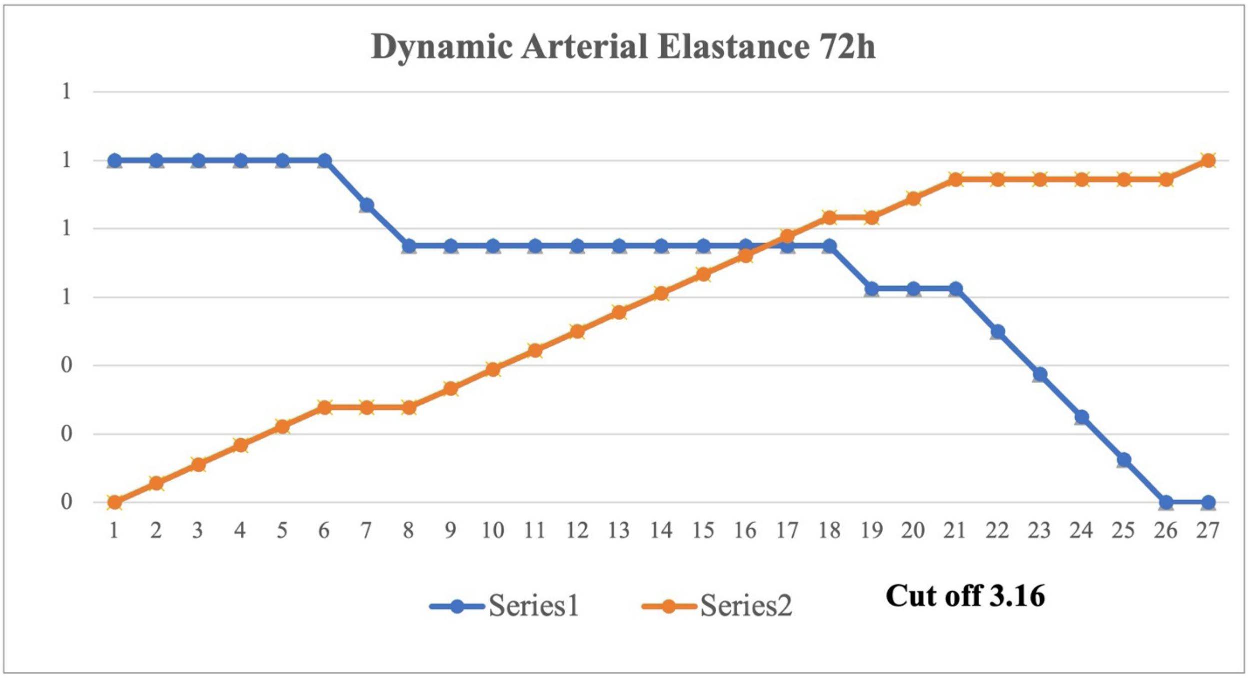
Legend: Eadyn=dynamic arterial elastance.

Figure 2. ROC analysis for dynamic arterial elastance in predicting mortality in septic shock



Legend: ROC=receiver operating characteristic; Ea=arterial elastance.

Figure 3. AUC analysis for dynamic arterial elastance in predicting mortality in septic shock



Legend: AUC=area under the curve.

References

1. Lee E-P, Wu H-P, Chan O-W, Lin J-J, Hsia S-H. Hemodynamic monitoring and management of pediatric septic shock. Biomed J 2022;45:63-73.
2. Antonelli M, Levy M, Andrews PJD, Chastre J, Hudson LD, Manthous C, et al. Hemodynamic monitoring in shock and implications for management. International Consensus Conference, Paris, France, 27–28 April 2006. Intensive Care Med 2007;33:575-90.
3. Ochagavía A, Baigorri F, Mesquida J, Ayuela JM, Ferrándiz A, García X, et al. Hemodynamic monitoring in the critically patient. Recomendations of the Cardiological Intensive Care and CPR Working Group of the Spanish Society of Intensive Care and Coronary Units. Med Intensiva 2014;38:154-69.
4. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med 2021;47:1181-247.
5. Pierrakos C, Velissaris D, Scolletta S, Heenen S, De Backer D, Vincent J-L. Can changes in arterial pressure be used to detect changes in cardiac index during fluid challenge in patients with septic shock? Intensive Care Med 2012;38:422-8.
6. Lakhal K, Ehrmann S, Perrotin D, Wolff M, Boulain T. Fluid challenge: tracking changes in cardiac output with blood pressure monitoring (invasive or non-invasive). Intensive Care Med 2013;39:1953-62.
7. Monge Garcia MI, Gil Cano A, Gracia Romero M. Dynamic arterial elastance to predict arterial pressure response to volume loading in preload-dependent patients. Crit Care 2011;15:R15.
8. Monge García MI, Gracia Romero M, Gil Cano A, et al. Dynamic arterial elastance as a predictor of arterial pressure response to fluid administration: a validation study. Crit Care 2014;18:626.
9. Monge Garcia MI, Guijo González P, Saludes Orduña P, Gracia Romero M, Gil Cano A, Messina A, et al. Dynamic Arterial Elastance During Experimental Endotoxic Septic Shock: A Potential Marker of Cardiovascular Efficiency. Front Physiol 2020;11:562824.
10. Setyaningtyas A, Soetjipto S, Endaryanto A, Pudjiadi AH. The Correlations of Human Atrial Natriuretic Peptide on Cardiac Function and Hemodynamics in Pediatric Septic Shock. Open Access Emerg Med 2022;14:525-34.
11. Wiguna Y, Setiawan P, Semedi BP, Purwanto B. Syndecan-1 Laktat dan Profil Lipid sebagai Faktor Risiko Keparahan dan Mortalitas Sepsis. Jurnal Anestesi Perioperatif 2021;9:18-26.
12. Monge Garcia MI, Jian Z, Settels JJ, Hatib F, Cecconi M, Pinsky MR. Reliability of effective arterial elastance using peripheral arterial pressure as surrogate for left ventricular end-systolic pressure. J Clin Monit Comput 2019;33:803-13.
13. Sunagawa K, Maughan WL, Burkhoff D, Sagawa K. Left ventricular interaction with arterial load studied in isolated canine ventricle. American Journal of Physiology-Heart and Circulatory Physiology 1983;245:H773-80.
14. Kelly RP, Ting CT, Yang TM, Liu CP, Maughan WL, Chang MS, et al. Effective arterial elastance as index of arterial vascular load in humans. Circulation 1992;86:513-21.
15. Segers P, Stergiopulos N, Westerhof N. Relation of effective arterial elastance to arterial system properties. Am J Physiol Heart Circ Physiol 2002;282:H1041-6.
16. Mahmood SS, Pinsky MR. Heart-lung interactions during mechanical ventilation: the basics. Ann Transl Med 2018;6:349.
17. Zanon F, Aggio S, Baracca E, Pastore G, Corbucci G, Boaretto G, et al. Ventricular-arterial coupling in patients with heart failure treated with cardiac resynchronization therapy: may we predict the long-term clinical response? Eur J Echocardiogr 2009;10:106-11.
18. Guinot PG, Abou-Arab O, Guilbart M, Bar S, Zogheib E, Daher M, et al. Monitoring dynamic arterial elastance as a means of decreasing the duration of norepinephrine treatment in vasoplegic syndrome following cardiac surgery: a prospective, randomized trial. Intensive Care Med 2017;43:643-51.
19. Monnet X, Letierce A, Hamzaoui O, Chemla D, Anguel N, Osman D, et al. Arterial pressure allows monitoring the changes in cardiac output induced by volume expansion but not by norepinephrine. Crit Care Med 2011;39:1394-9.
20. Lee J-H, Kwon Y-L, Na J-H, Jang Y-E, Kim E-H, Kim H-S, et al. Is dynamic arterial elastance a predictor of an increase in blood pressure after fluid administration in pediatric patients with hypotension? Reanalysis of prospective observational studies. Pediatr Anaesthe 2020;30:34-42.
21. Guinot P-G, Huette P, Bouhemad B, Abou-Arab O, Nguyen M. A norepinephrine weaning

strategy using dynamic arterial elastance is associated with reduction of acute kidney injury in patients with vasoplegia after cardiac surgery: A post-hoc analysis of the randomized SNEAD study. J Clin Anesth 2023;88:111124.
22. Guarracino F, Baldassarri R, Pinsky MR. Ventriculo-arterial decoupling in acutely altered hemodynamic states. Crit Care 2013;17:213.
23. Lamia B, Chemla D, Richard C, Teboul J-L. Clinical review: Interpretation of arterial pressure wave in shock states. Crit Care 2005;9:601-6.

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