CLINICAL CASE

Olfa Hamzaoui
Medical ICU
Teaching Hospital of Reims
France

EMA-AT00-230024

Conflicts of Interest

- I have received honoraria from Baxter
- I have no conflicts of interest relevant to the content of this presentation
- I solely and independently prepared the content of this presentation
- The information shared in this webinar and presentation reflects my personal views and not necessarily those of Baxter.
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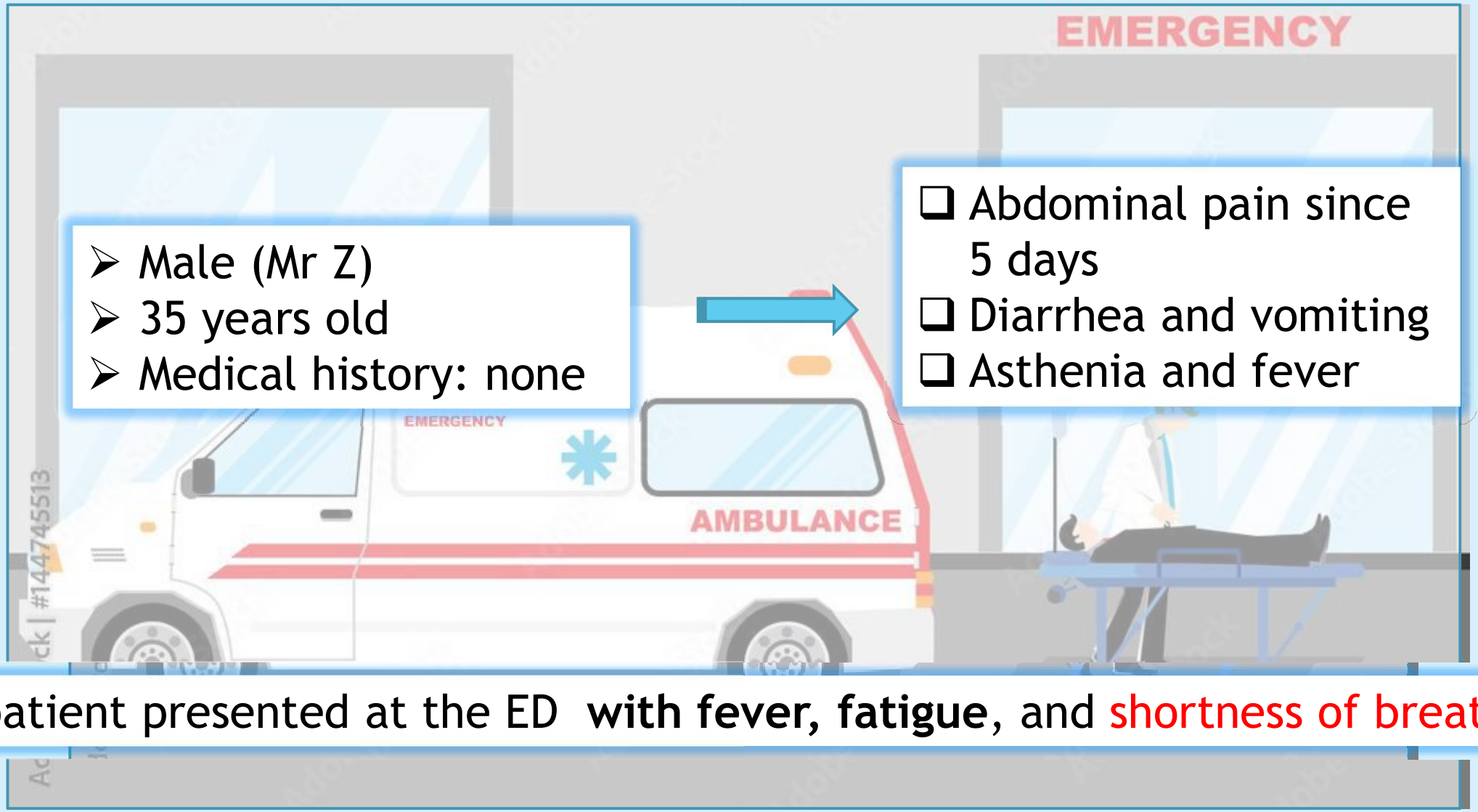
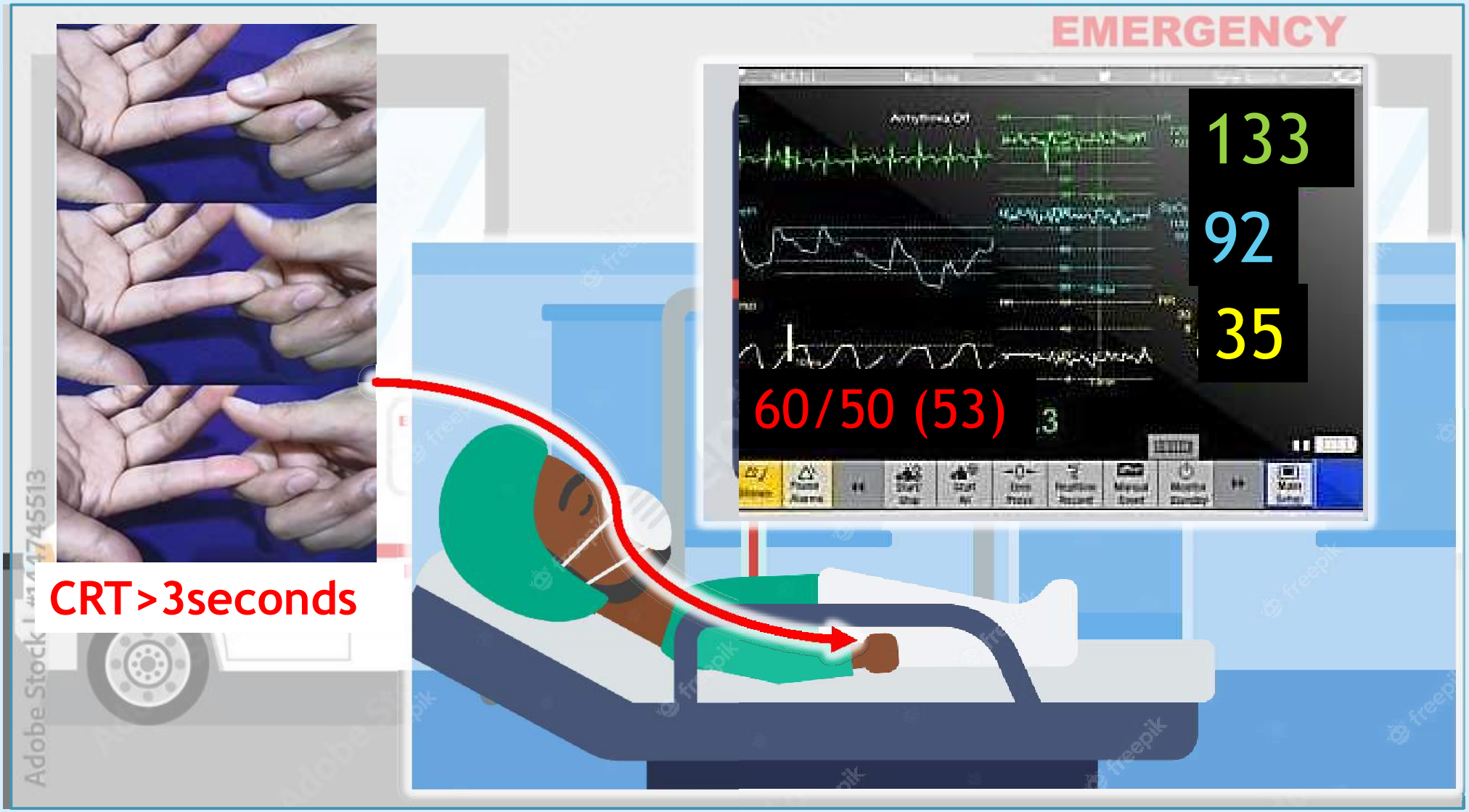


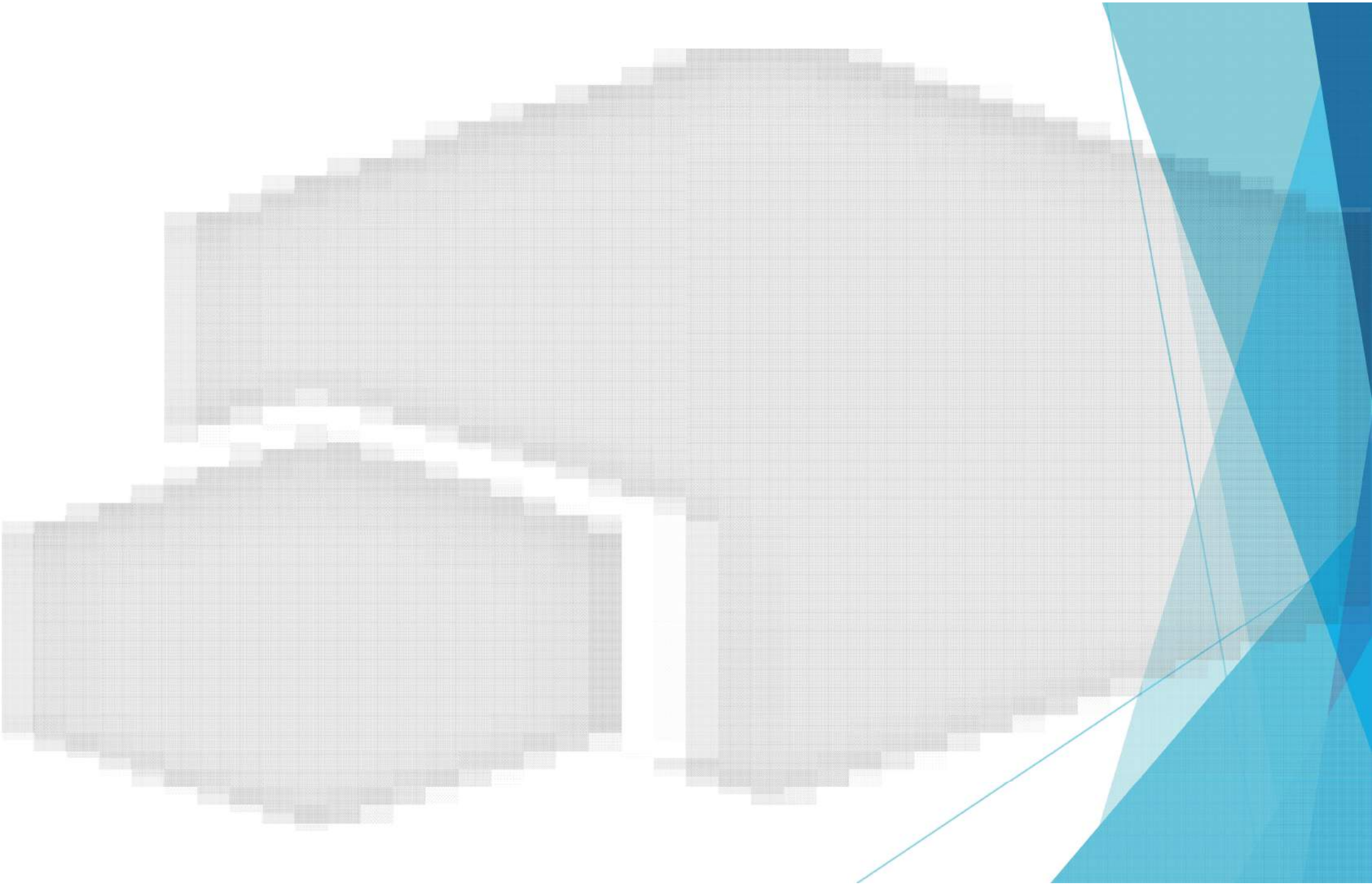
- Male (Mr Z)
- 35 years old
- Medical history: none

- ❑ Abdominal pain since 5 days
- ❑ Diarrhea and vomiting
- ❑ Asthenia and fever

he patient presented at the ED **with fever, fatigue**, and shortness of breath

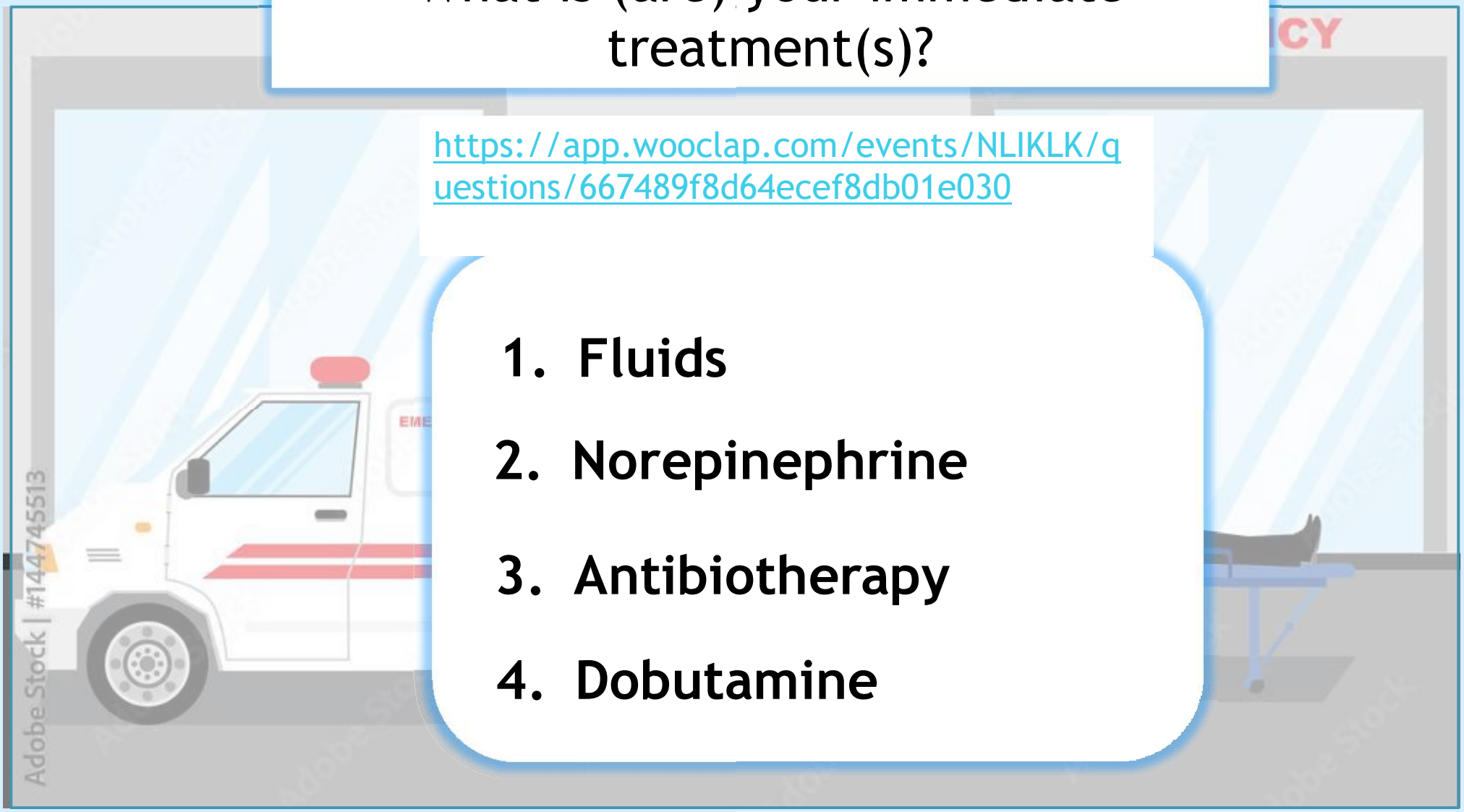

EMERGENCY
133
92
35
60/50 (53)
CRT>3seconds


EMERGENCY
Quitter
Comment participer ?
UNIVERSITÉ DE REIMS CHAMPAGNE-ARDENNE
1 Allez sur wooclap.com
2 Entrez le code d'événement dans le bandeau supérieur
Code d'événement
NLIKLK
1 Envoyez @NLIKLK au 06 44 60 96 62
2 Vous pouvez participer
Désactiver les réponses par SMS

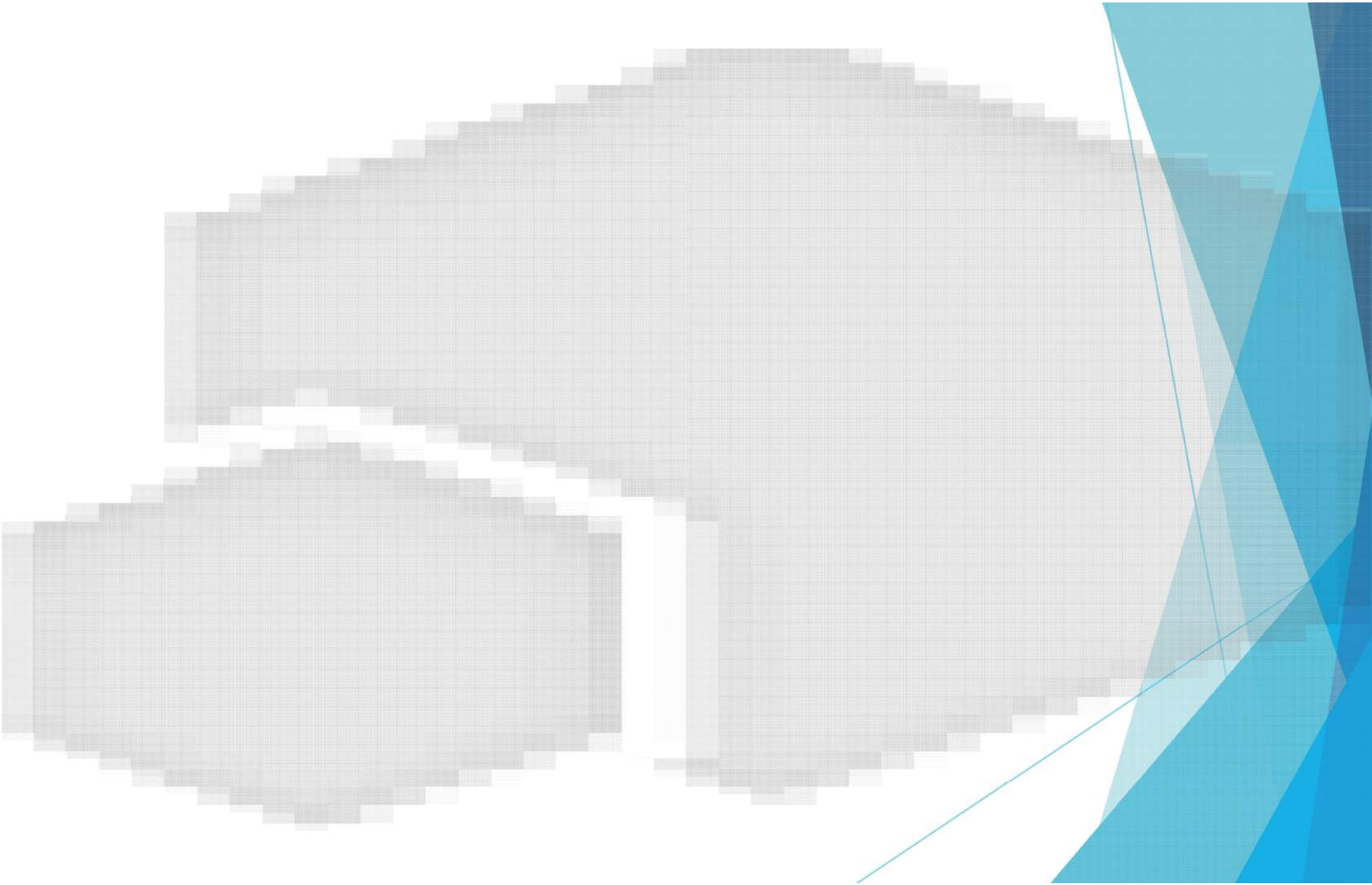


What is (are) your immediate treatment(s)?

https://app.wooclap.com/events/NLIKLK/questions/667489f8d64ecef8db01e030

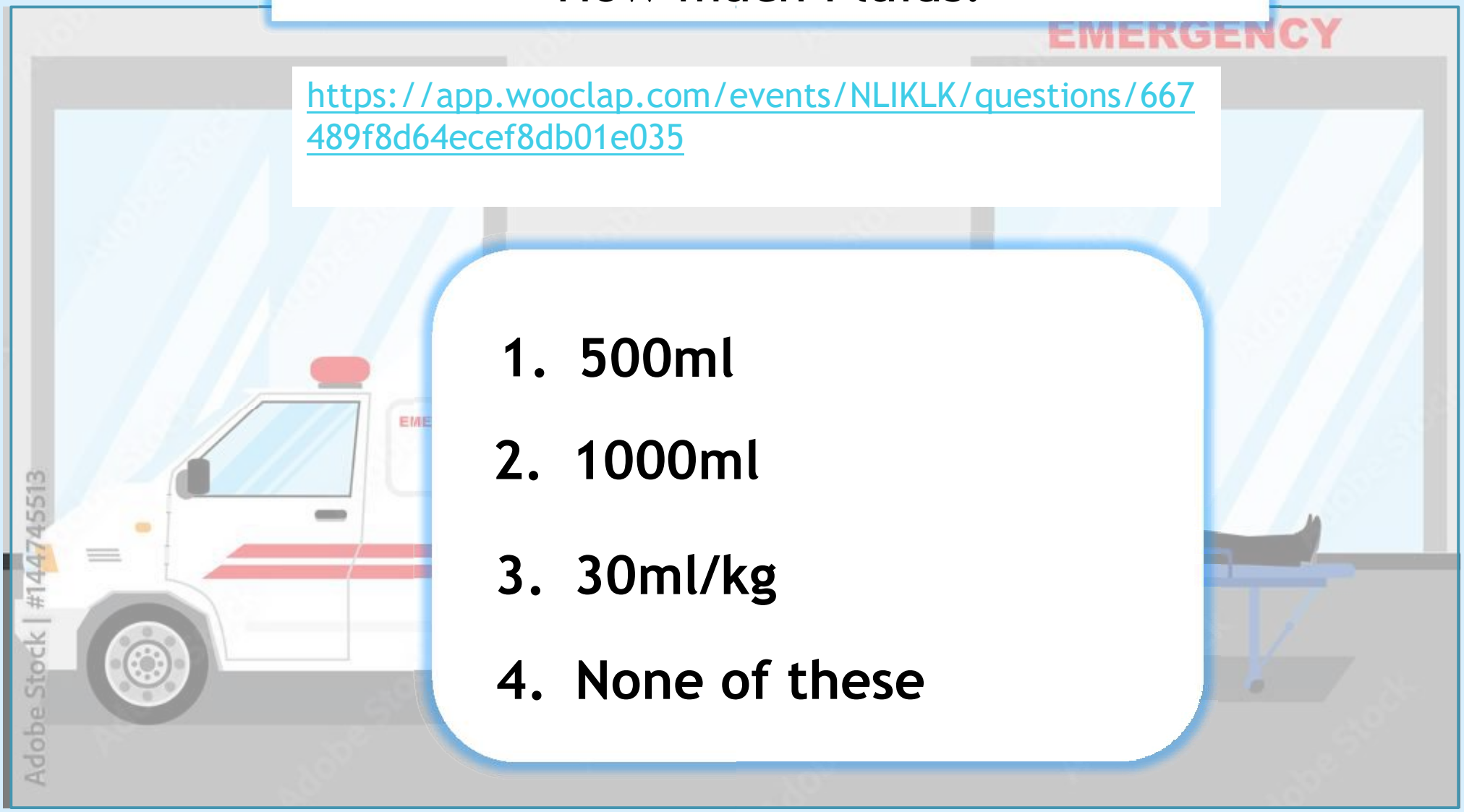


1. **Fluids**
2. **Norepinephrine**
3. **Antibiotherapy**
4. **Dobutamine**



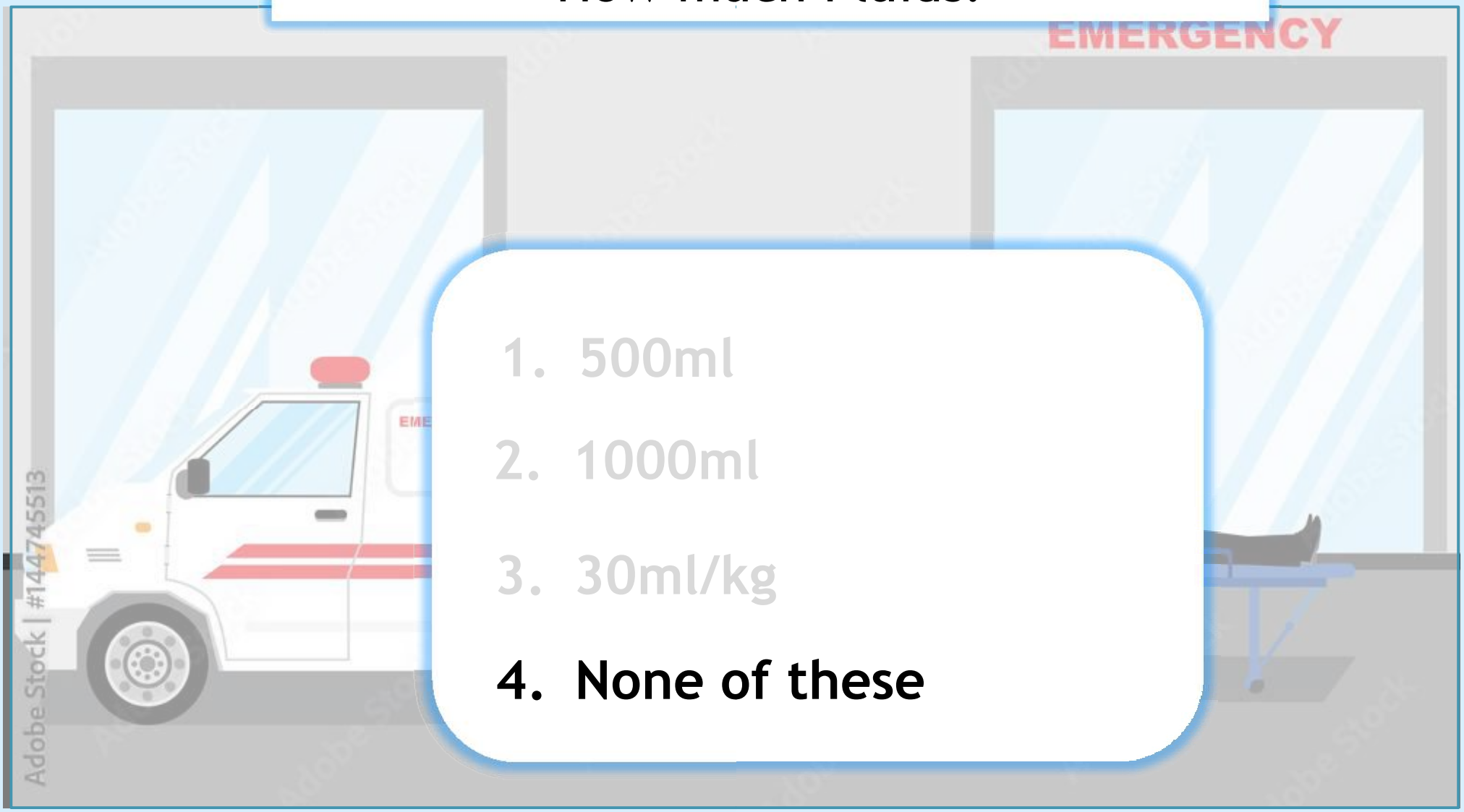
How much Fluids?

https://app.wooclap.com/events/NLIKLK/questions/667489f8d64ecef8db01e035



1. 500ml
2. 1000ml
3. 30ml/kg
4. None of these

How much Fluids?



1. 500ml
2. 1000ml
3. 30ml/kg
4. **None of these**

GUIDELINES

Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021

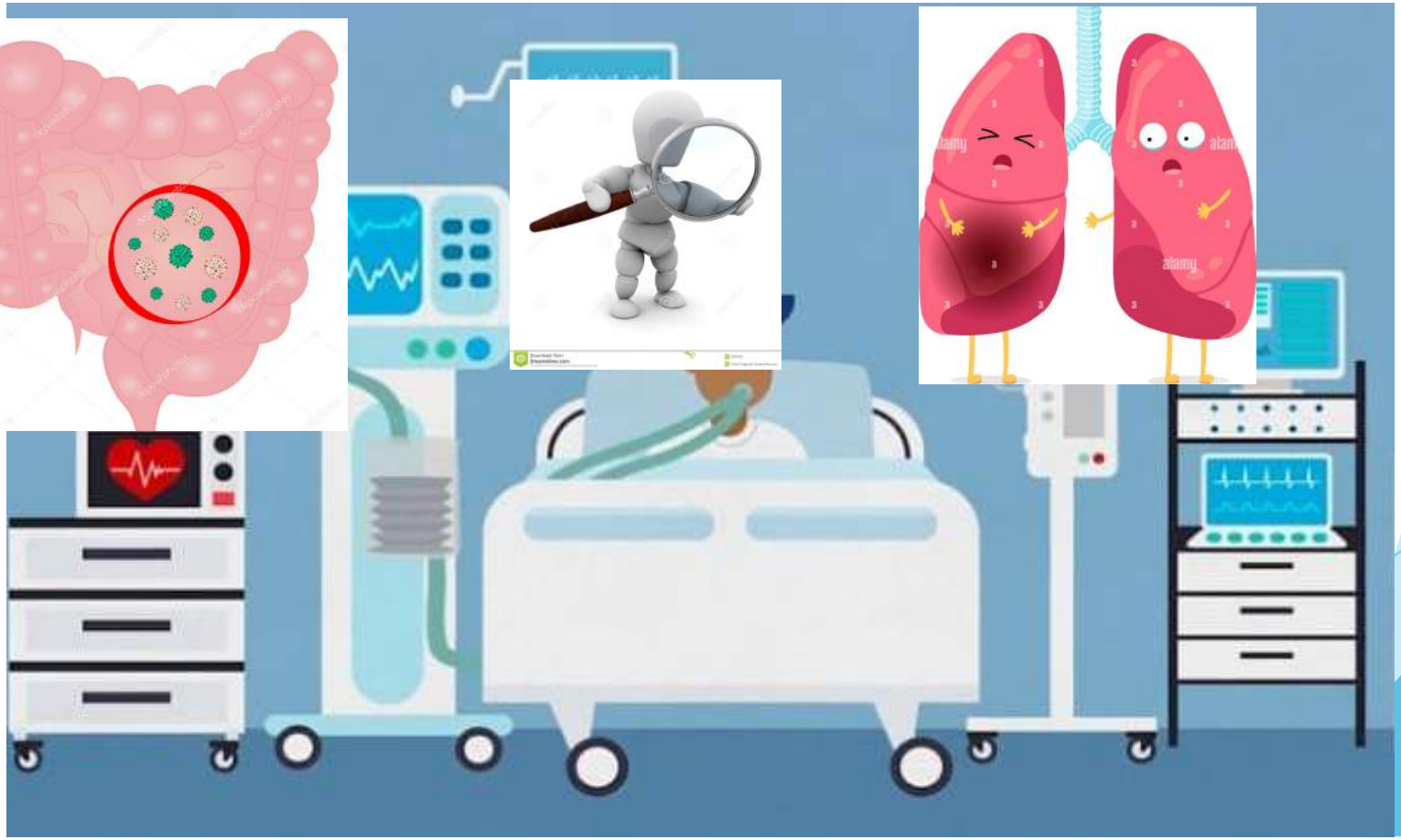
Intensive Care Med (2021) 47:1181–1247

LOW

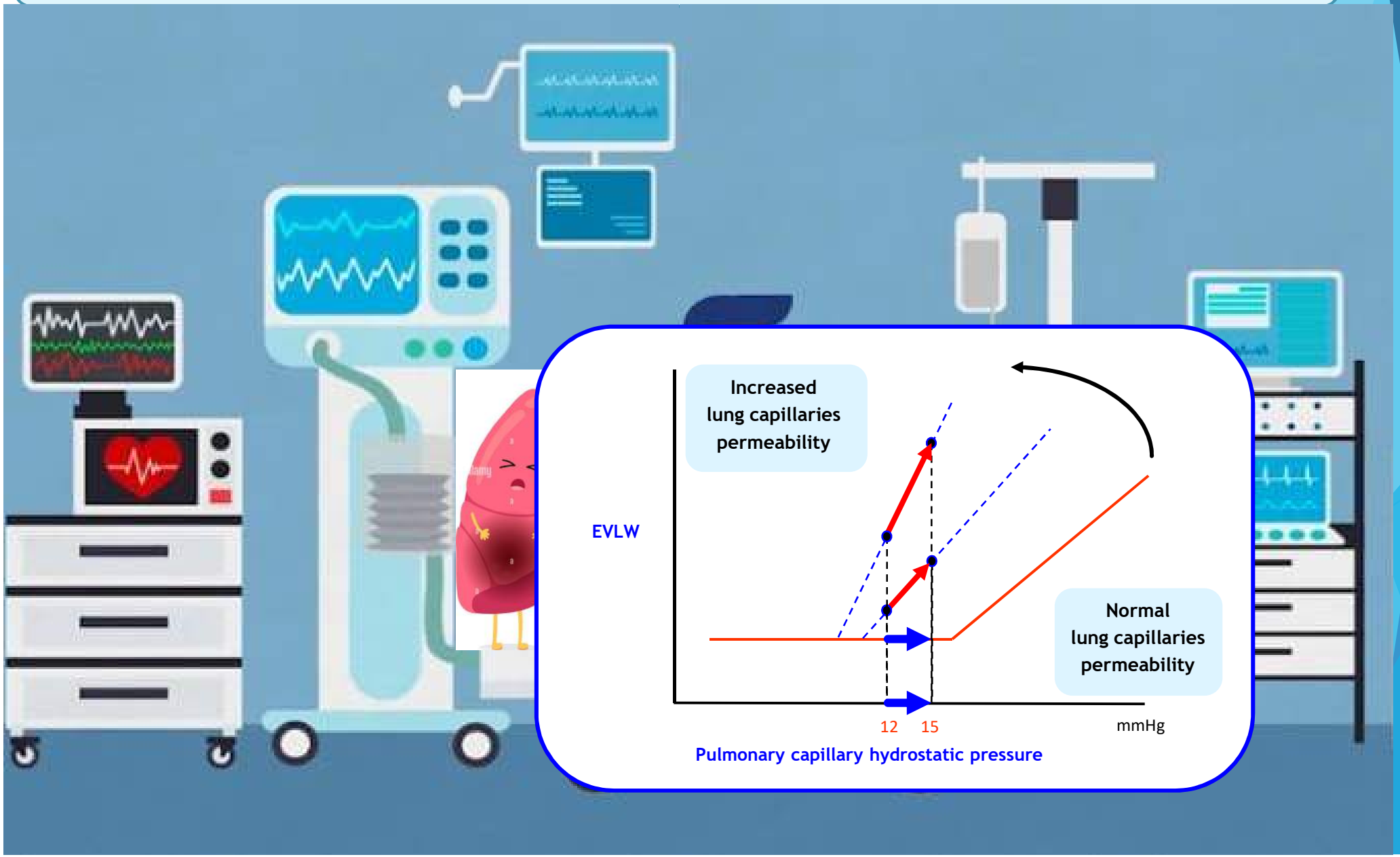
5 For patients with sepsis induced hypoperfusion or septic shock we **suggest** that at least 30 mL/kg of intravenous (IV) crystalloid fluid should be given within the first 3 hours of resuscitation.

> ***2016 STATEMENT***
>
> *"We **recommend** that in the initial resuscitation from sepsis-induced hypoperfusion, at least 30ml/kg of intravenous crystalloid fluid be given within the first 3 hours."*

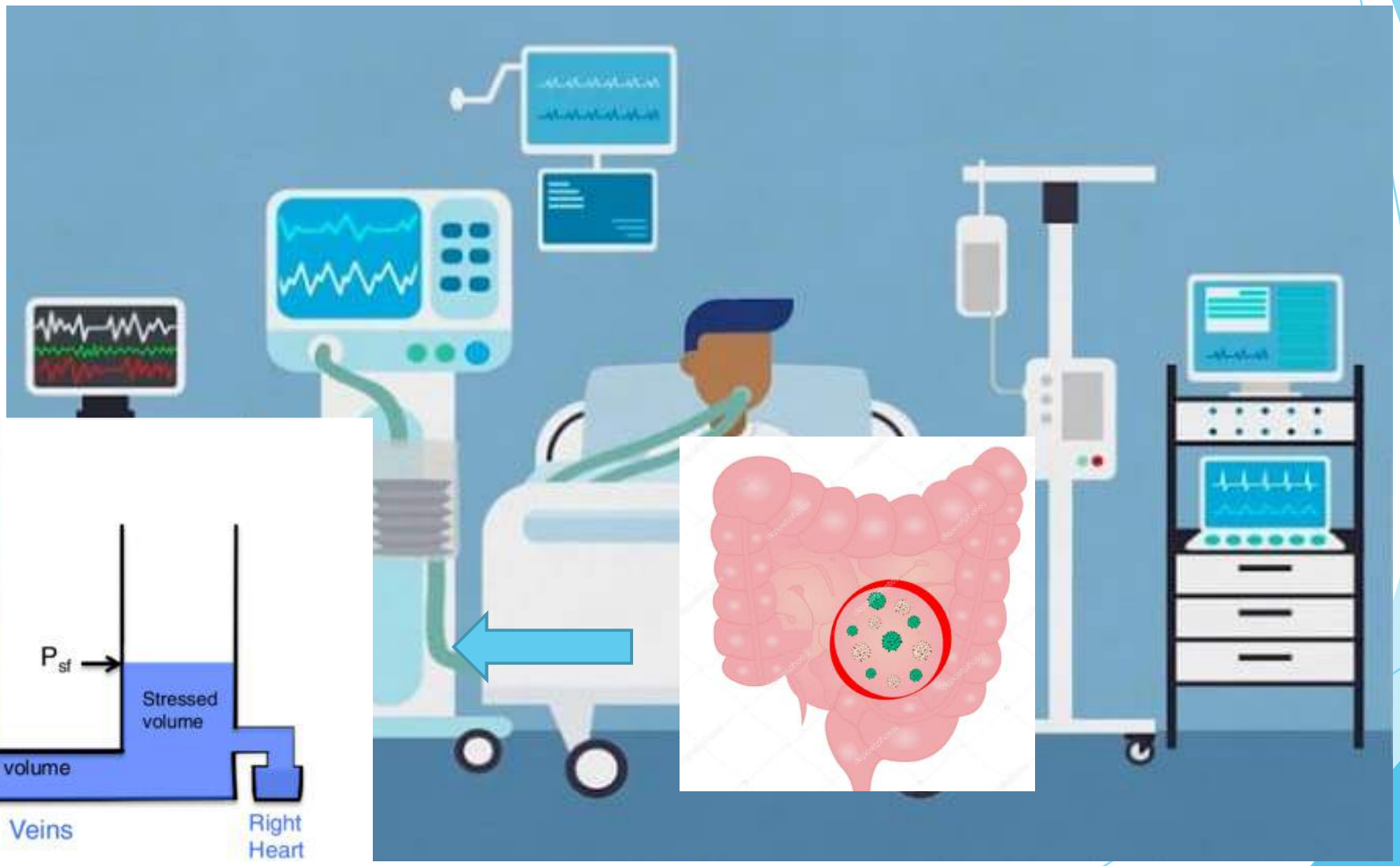
No evidence?



Pneumonia: relative hypovolemia and increased capillary leak

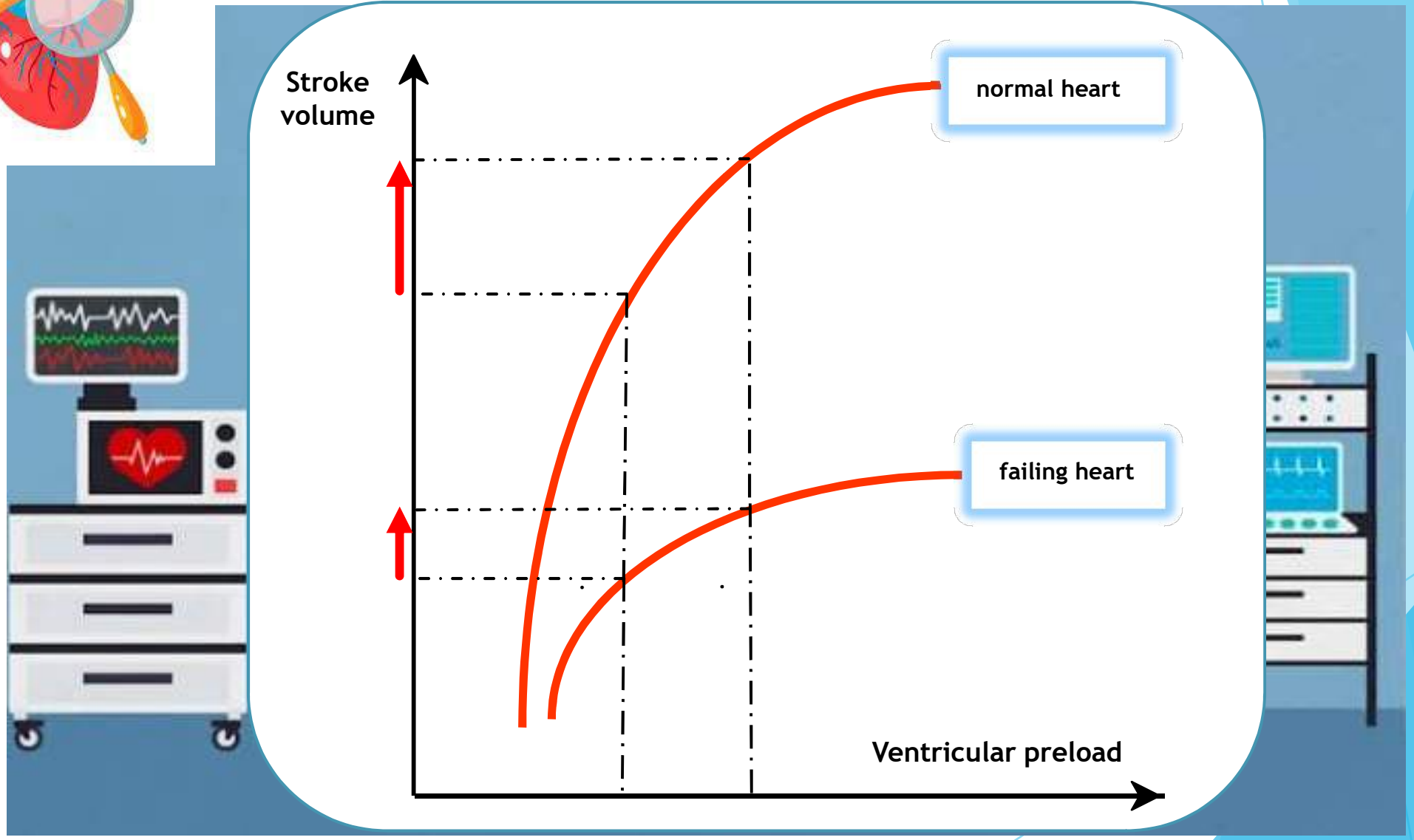


Peritonitis or abdominal sepsis: severe absolute hypovolemia



HEART RESEARCH

cardiac dysfunction: yes or no?



EDITORIAL Open Access

Equilibrating SSC guidelines with individualized care

Jean-Louis Vincent[1*], Mervyn Singer[2], Sharon Einav[3], Rui Moreno[4], Julia Wendon[5], Jean-Louis Teboul[6], Jan Bakker[7,8,9,10], Glenn Hernandez[11], Djillali Annane[12], Angélique M. E. de Man[13], Xavier Monnet[14], V. Marco Ranieri[15], Olfa Hamzaoui[16], Jukka Takala[17], Nicole Juffermans[18,19], Jean-Daniel Chiche[20], Sheila N. Myatra[21] and Daniel De Backer[22]

Critical Care (2021) 25:397

2 Initial resuscitation

We recommend **individualizing** initial fluid resuscitation. No single formula can be applied to all patients, as **fluid requirements vary** substantially (depending on the source of sepsis and preexis cardiovascular function).

Fluid resuscitation during early sepsis: a need for individualization

Mathieu JOZWIAK [1, 2], Olfa HAMZAOUI [3], Xavier MONNET [1, 2], Jean-Louis TEBOUL [1, 2] *

Minerva Anestesiologica 2018 August;84(8):987-92

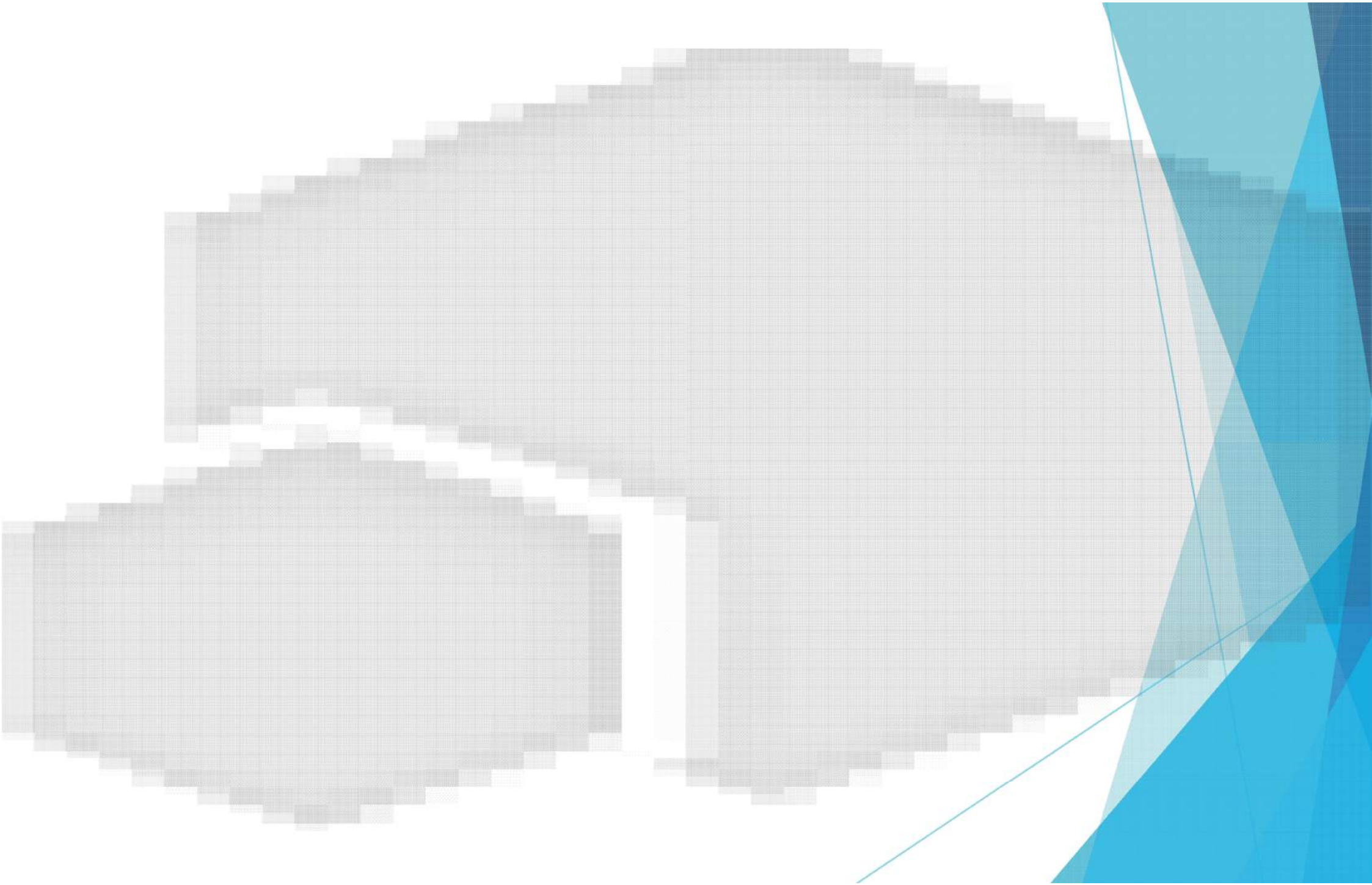
Pt presenting with **septic shock**

Infuse around **10 mL/kg** crystalloids within the **first hour**

Decrease infusion rate if:
. Worsening of tachypnea
. Fall in O_2 saturation

Increase infusion rate if:
. Fluid losses
. Abdominal sepsis
. Mottling or ↗ CRT
. Low PP

Importance of **individualizing** the initial **fluid therapy**



Fluids: How can you assess the effectiveness?

https://app.wooclap.com/events/NLIKLK/questions/667489f8d64ecef8db01e03a

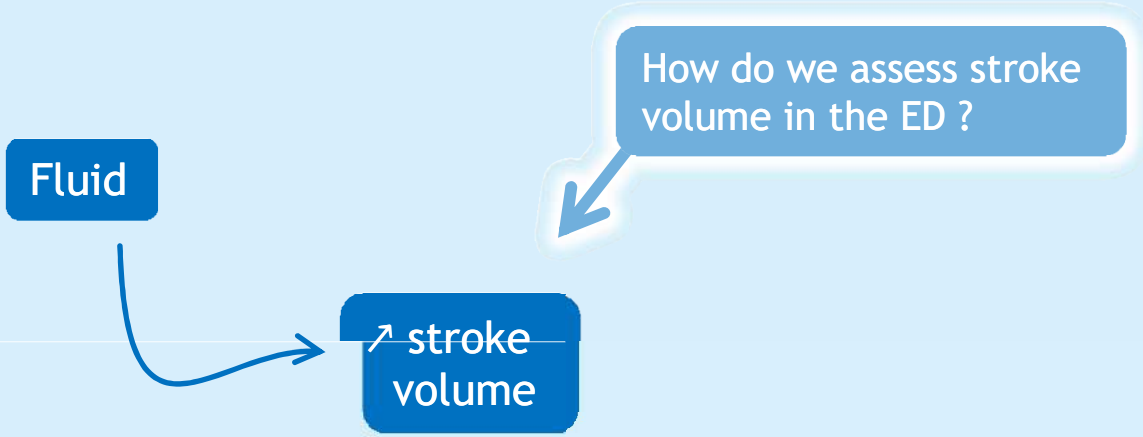
1. Mean arterial pressure
2. Pulse Pressure
3. Diastolic arterial pressure
4. Capillary refill time: CRT

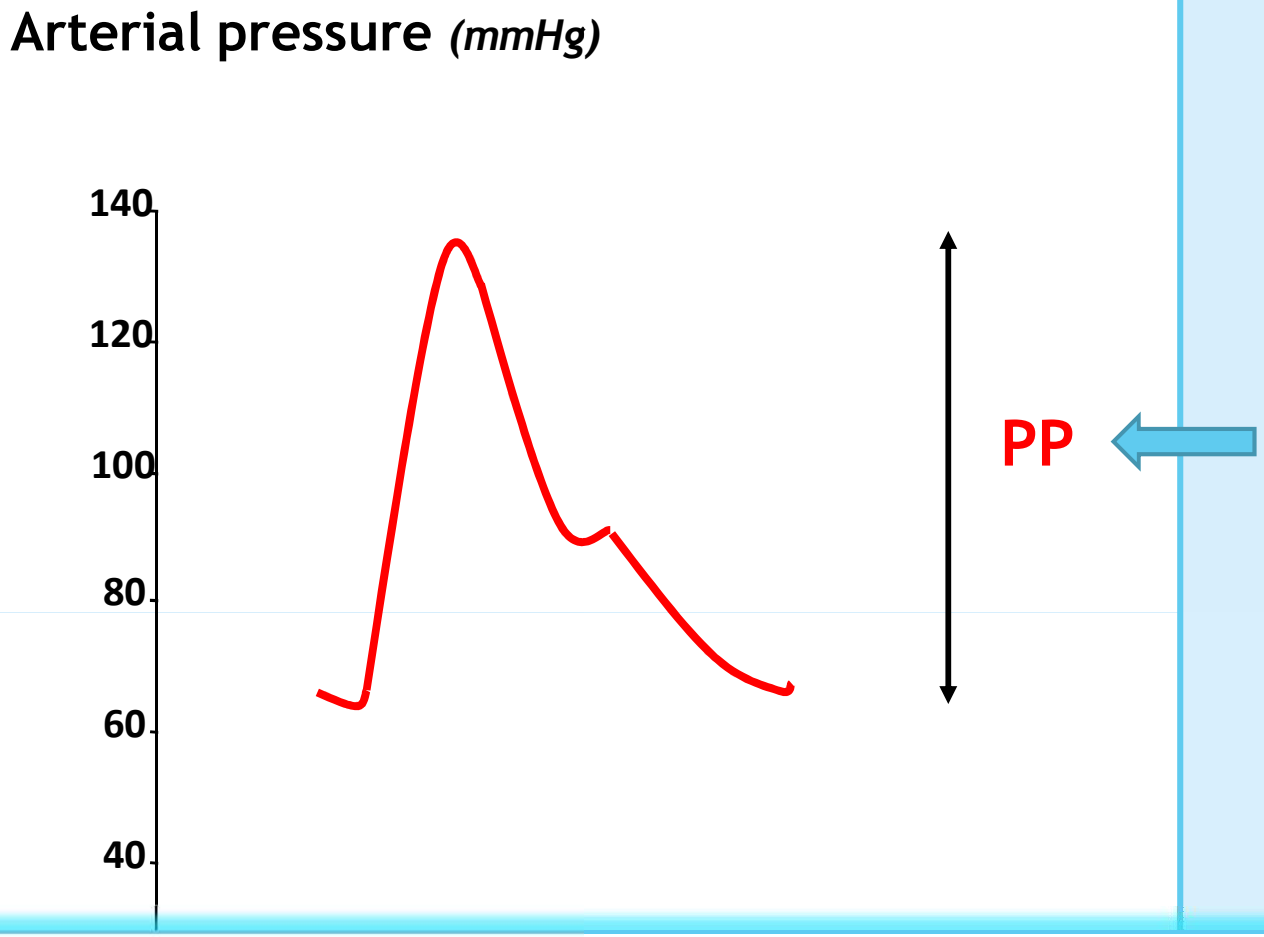
Fluids: How can you assess the effectiveness?

Q3

1. Mean arterial pressure
2. **Pulse Pressure**
3. Diastolic arterial pressure
4. **Capillary refill time: CRT**

Fluids: How can you assess the effectiveness?





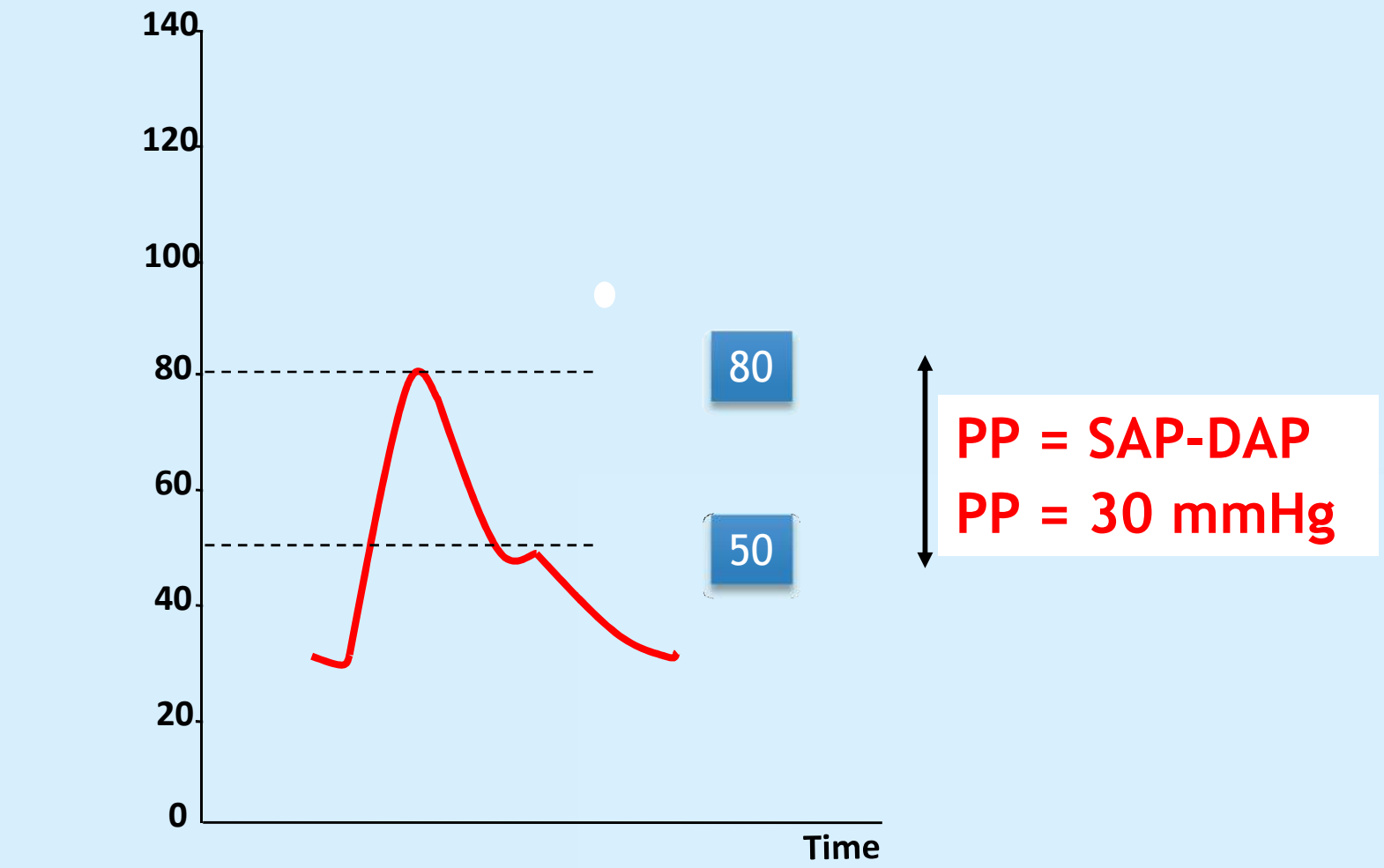
Aortic pulse pressure = SV / aortic compliance

Chemla et al AJP 1998

at the **Emergency Department**

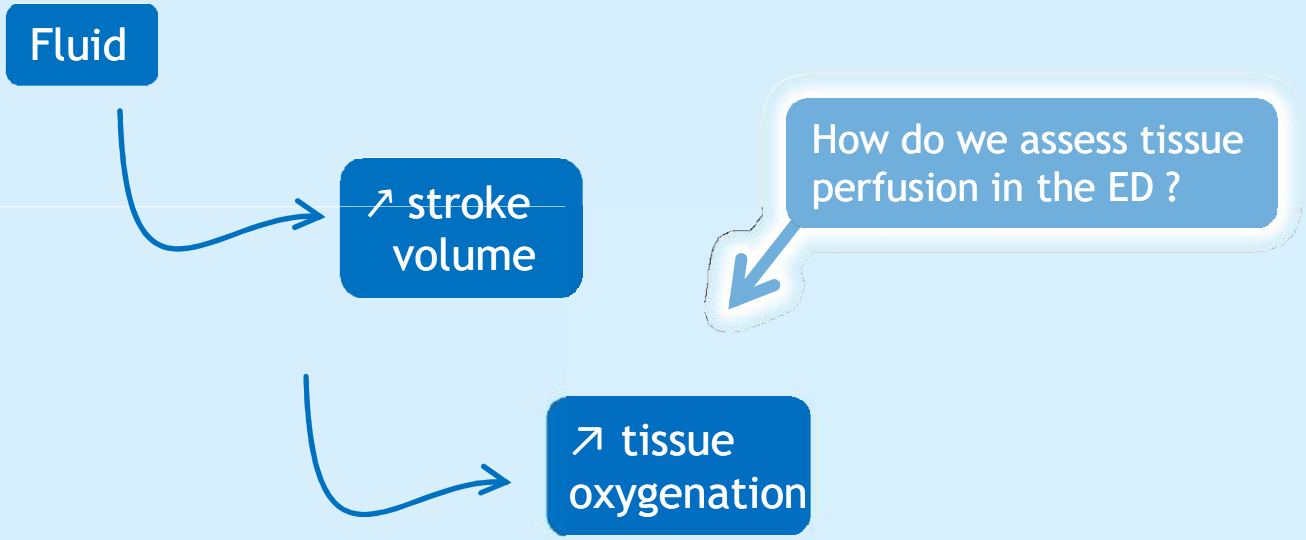
- Abdominal tenderness
- Mottling and clammy skin
- Fever (38.5°C)
- Increased capillary refill time

- Respiratory rate = 25 /min
- Heart rate = 120 /min
- **BP = 80/50 (60) mmHg**
- SpO_2 = 100%



a low PP reflects a low stroke volume

Fluids: How can you assess the effectiveness?



Fluids: How can you assess the effectiveness?

Multiple choice

1. Mean arterial pressure
2. **Pulse Pressure**
3. Diastolic arterial pressure
4. **Capillary refill time: CRT**

Kattan et al. Ann. Intensive Care (2020) 10:114
https://doi.org/10.1186/s13613-020-00732-1

Annals of Intensive Care

RESEARCH Open Access

A lactate-targeted resuscitation strategy may be associated with higher mortality in patients with septic shock and normal capillary refill time: a post hoc analysis of the ANDROMEDA-SHOCK study

Eduardo Kattan[1], Glenn Hernández[1], Gustavo Ospina-Tascón[2], Emilio Daniel Valenzuela[1], Jan Bakker[1,3,4,5], Ricardo Castro[1*] and The ANDROMEDA-SHOCK Study Investigators and the Latin America Intensive Care Network (LIVEN)

- **The ANDROMEDA-SHOCK trial** compared **CRT**-*vs.* **lactate**-targeted resuscitation in early SS
- ANDROMEDA-SHOCK study included 424 patients
- 378 patients had available data at 2 h

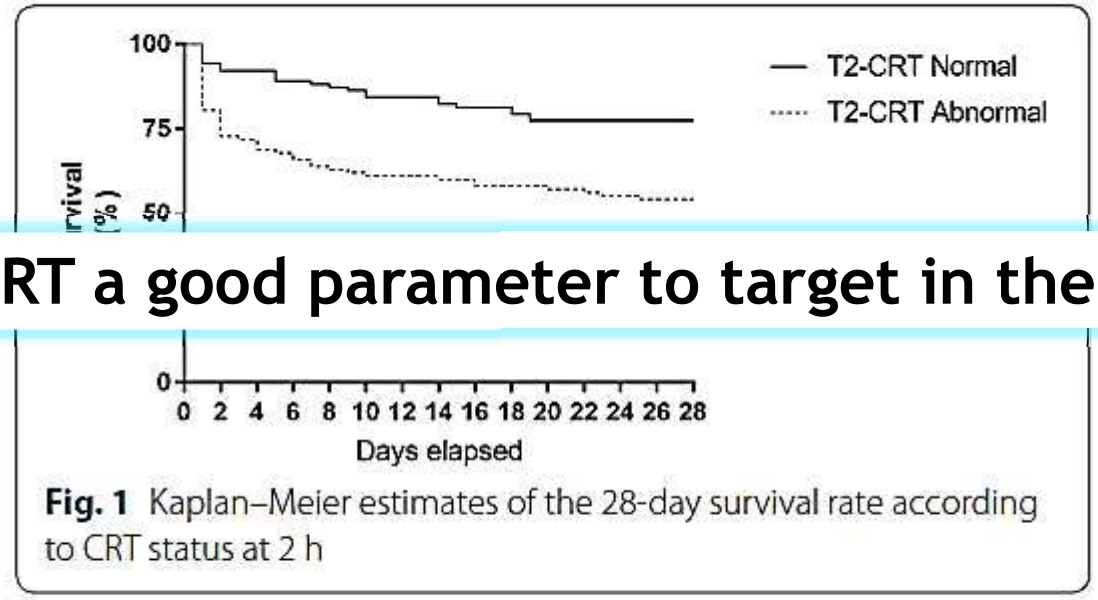
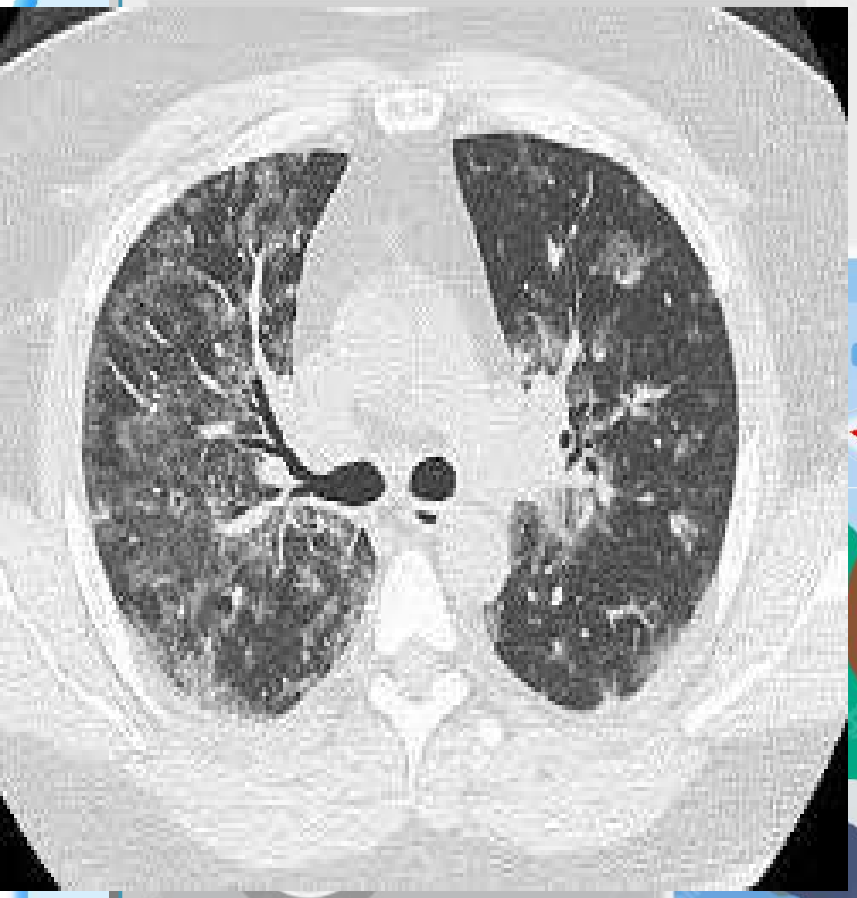


Fig. 1 Kaplan–Meier estimates of the 28-day survival rate according to CRT status at 2 h

CRT a good parameter to target in the ED

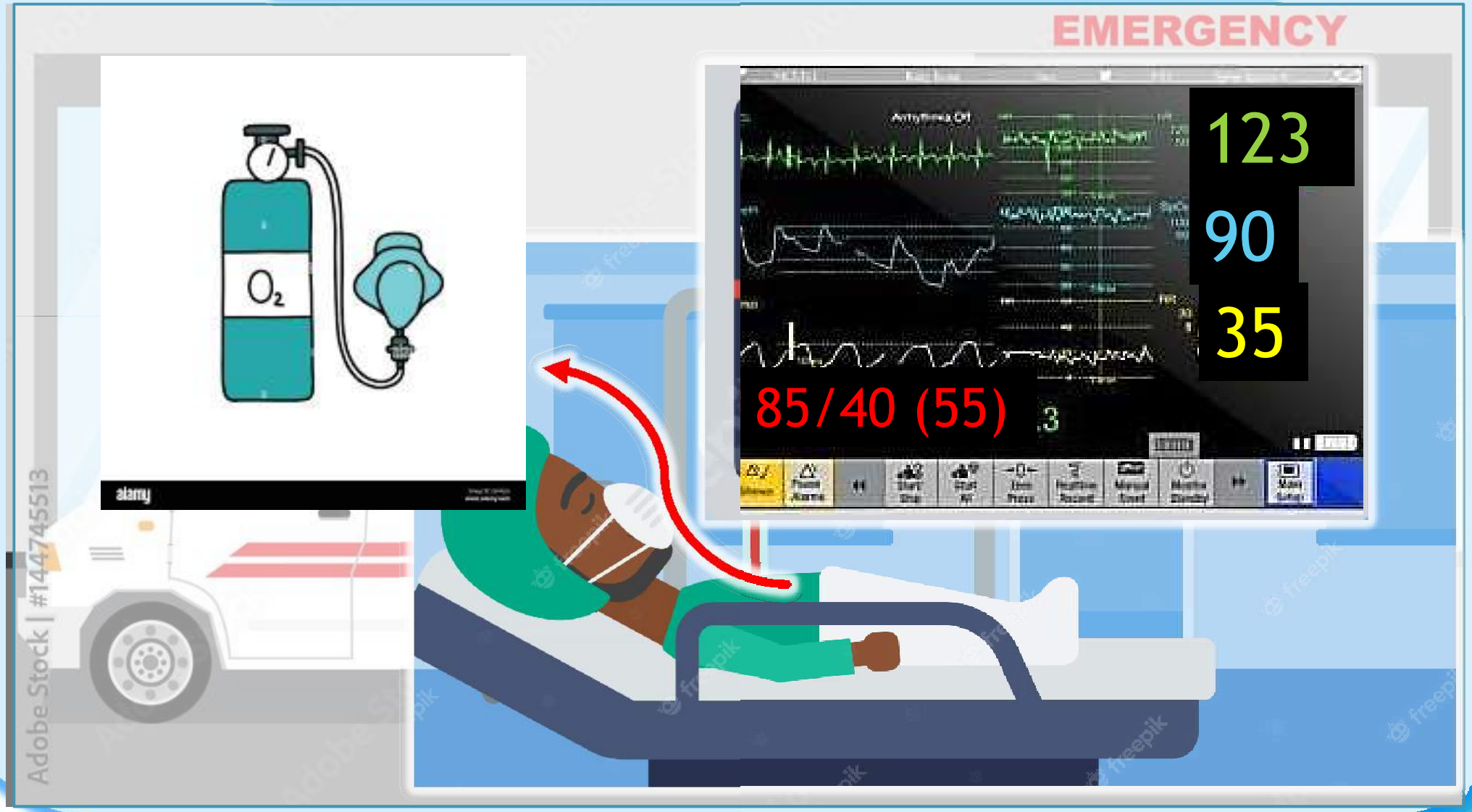
Regardless of the study group allocation, patients with **normal CRT** at **2 Hours,** had a **lower mortality** at **D28** compared to patients with **abnormal CRT** at T2

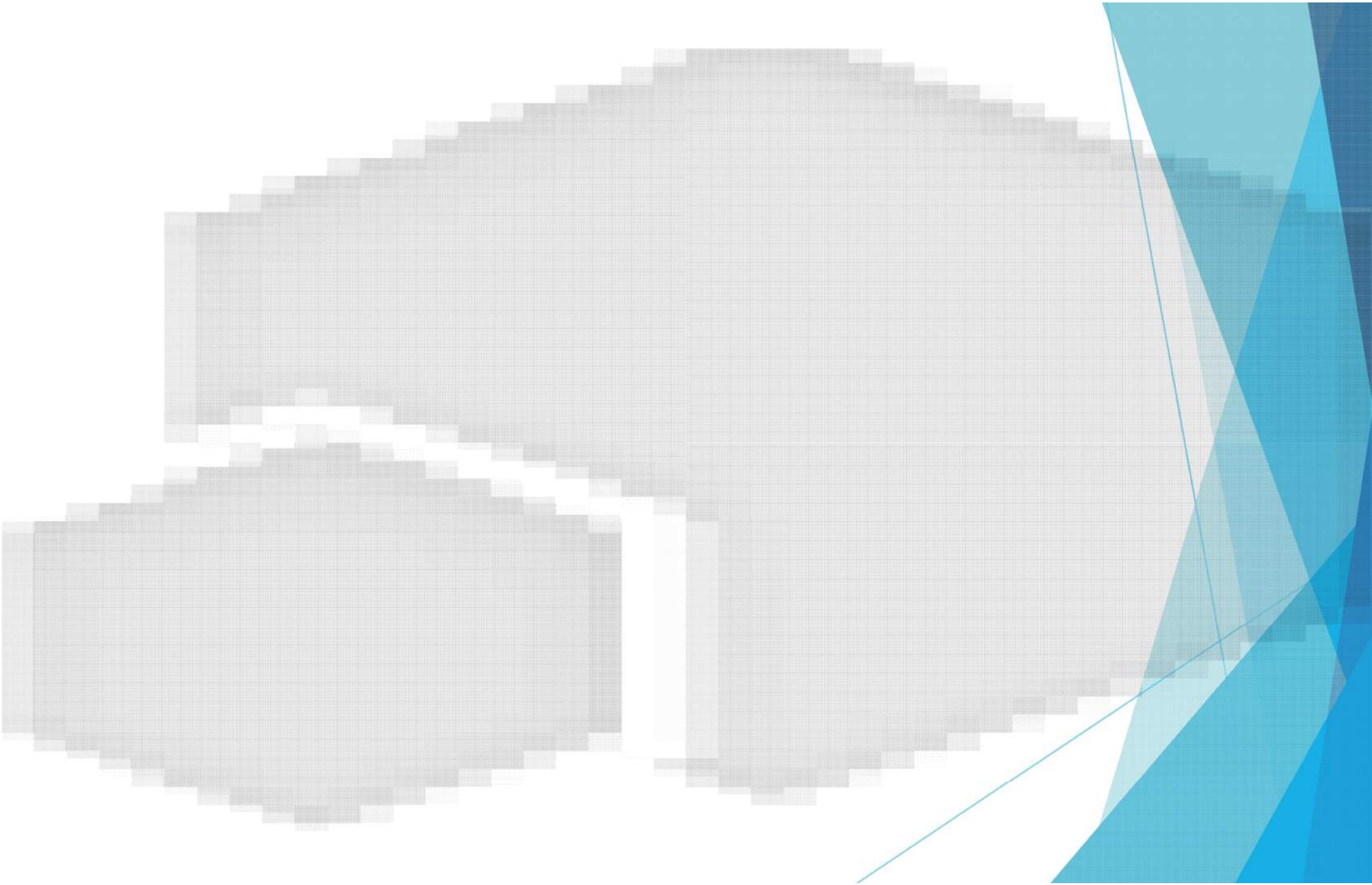
They received less resuscitative interventions and evolved with **lower SOFA** at 24h



- RT-PCR SARS-CoV-2: positive

He had 30ml/Kg of fluids and antibiotherapy





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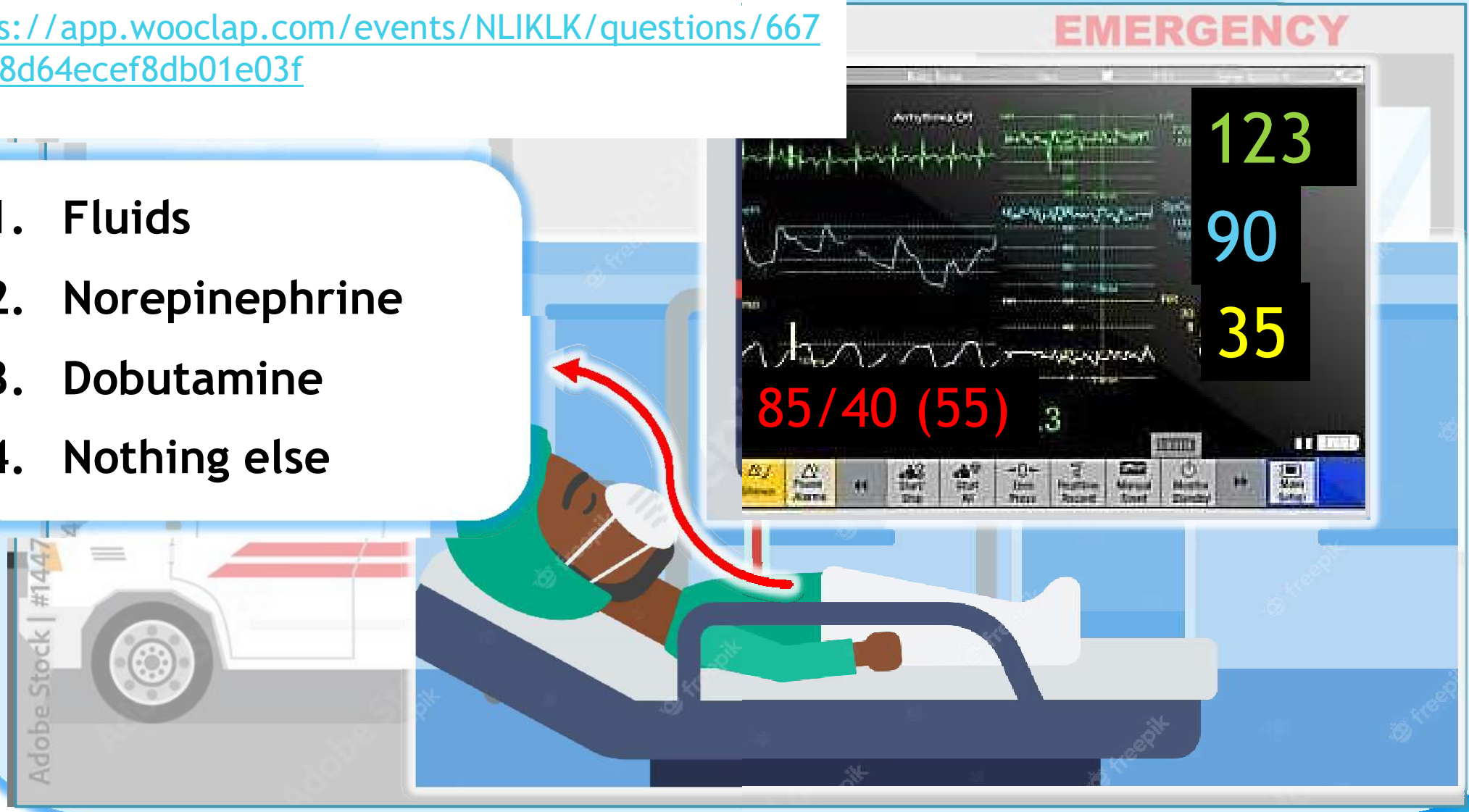
https://app.wooclap.com/events/NLIKLK/questions/667489f8d64ecef8db01e03f

1. Fluids
2. Norepinephrine
3. Dobutamine
4. Nothing else



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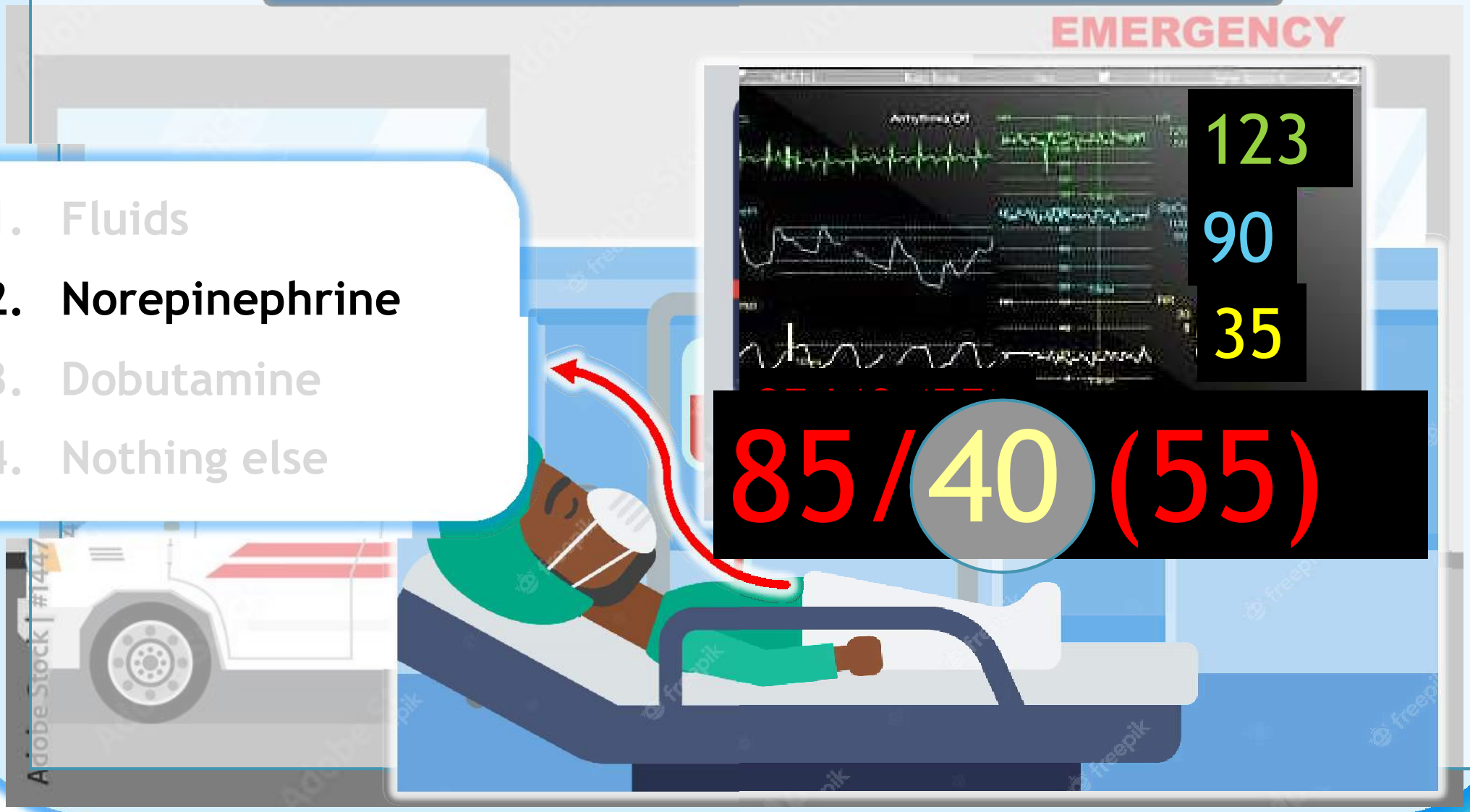
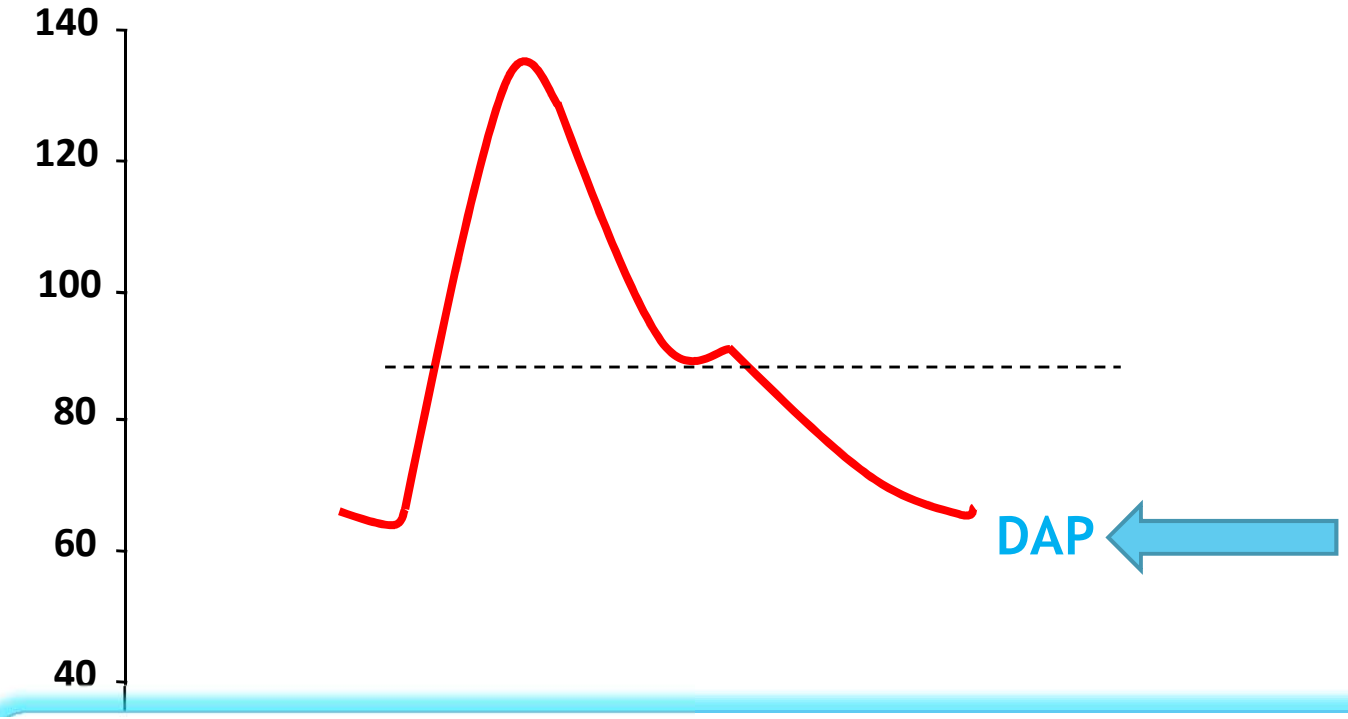


Pression artérielle*(mmHg)*



DAP is determined by :

- Vasomotor tone**: it reflects vasomotor tone**

Review Article

Early norepinephrine use in septic shock

Olfa Hamzaoui[1], Rui Shi[2,3]

Thorac Dis 2020;12(Suppl 1):S72-S77

Table 1 Arguments in favor of the early use of norepinephrine in septic shock

Consequences of early use of norepinephrine	Rational	References
Prevention of prolonged severe hypotension	Septic shock is characterized by a depressed arterial tone. fluid administration alone cannot be sufficient to correct severe hypotension	(10,11)
Increase in cardiac output	Increase in cardiac preload due to an increase in stressed blood volume	(12-16)
	Increase in cardiac contractility	(17)
Improvement of microcirculation	Improvement of microvascular blood flow in pressure-dependent vascular beds through increase in MAP in severely hypotensive patients	(13)
Prevention of fluid overload	Early administration of norepinephrine limits the volume of fluids infused	(18)
Improvement of outcome	Likely in relation to the preceding effects	(18,19)

Critical Care 2010, **14**:R142

RESEARCH Open Access

Early administration of norepinephrine increases cardiac preload and cardiac output in septic patients with life-threatening hypotension

Olfa Hamzaoui, Jean-François Georger, Xavier Monnet, Hatem Ksouri, Julien Maizel, Christian Richard, Jean-Louis Teboul*

- **NE** increases **preload**
- **NE decreases** the degree of **preload dependency**

Exactly like fluids !

By **redistributing the "non stressed" volume** into the **"stressed"** volume

Without infusing fluids!

Review Article

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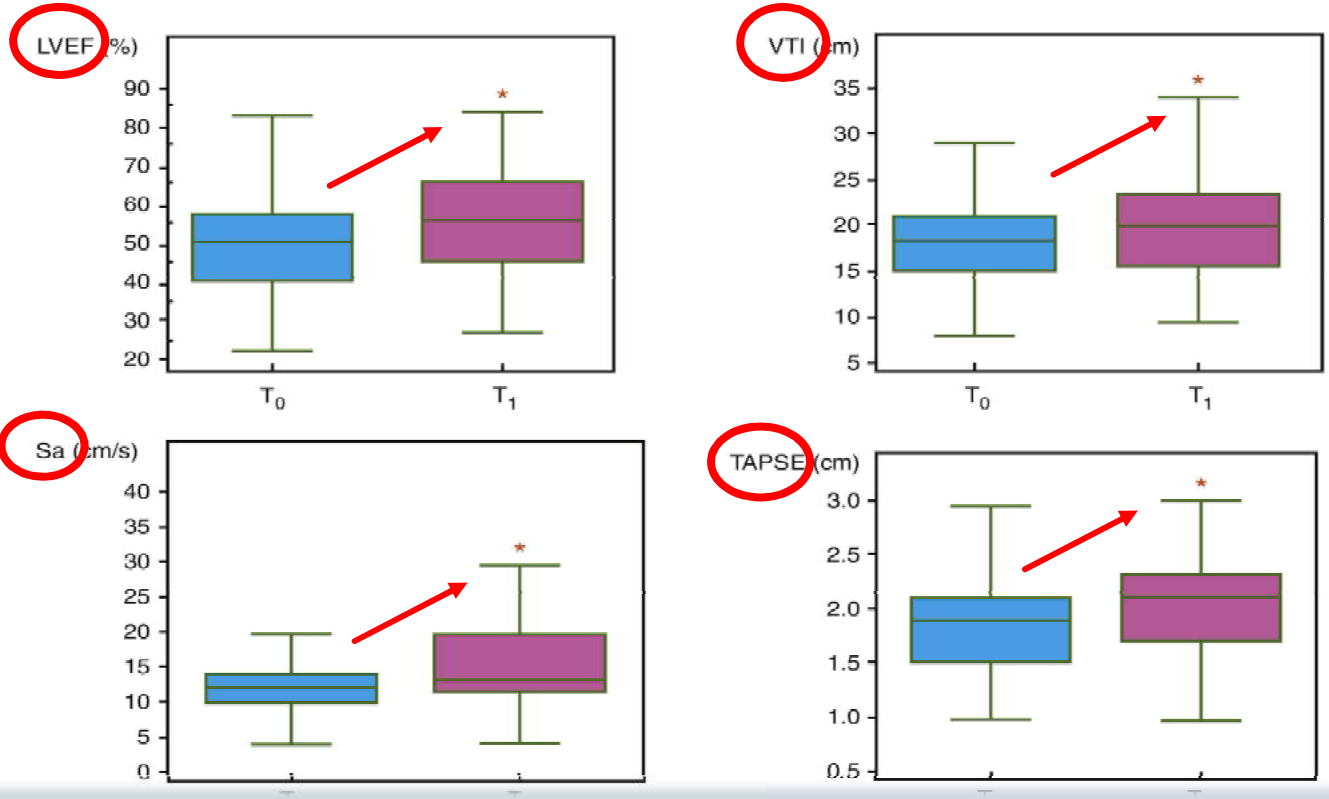
CLINICAL INVESTIGATION

Norepinephrine exerts an inotropic effect during the early phase of human septic shock

O. Hamzaoui[1,*], M. Jozwiak[2], T. Geffriaud[2], B. Sztrymf[1], D. Prat[1], F. Jacobs[1], X. Monnet[2], P. Trouiller[1], C. Richard[2] and J.L. Teboul[2]

British Journal of Anaesthesia, 120 (3): 517–524 (2018)

- 38 septic shock pts
- resuscitated < 3 hrs and with MAP< 65mmHg
- Repeated TTE



In spite of the **increase** in **LV afterload**, all the indices of **systolic function improved** with early **NE** suggesting an **improved cardiac contractility**

Review Article

Early norepinephrine use in septic shock

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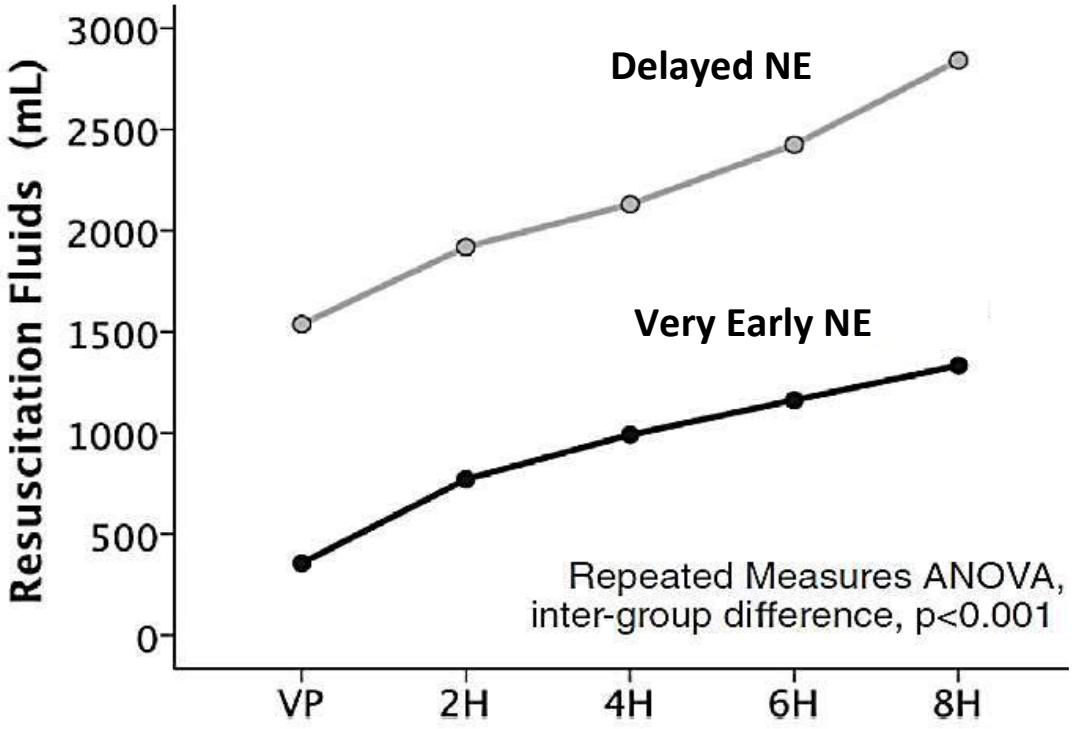
Effects of very early start of norepinephrine in patients with septic shock: a propensity score-based analysis

Gustavo A. Ospina-Tascón[1,2*], Glenn Hernandez[3], Ingrid Alvarez[1], Luis E. Calderón-Tapia[1], Ramiro Manzano-Nunez[1], Alvaro I. Sánchez-Ortiz[1], Egardo Quiñones[1], Juan E. Ruiz-Yucuma[1], José L. Aldana[1,2], Jean-Louis Teboul[4], Alexandre Biasi Cavalcanti[5], Daniel De Backer[6] and Jan Bakker[3,7,8,9]

Critical Care (2020) 24:52



Review Article

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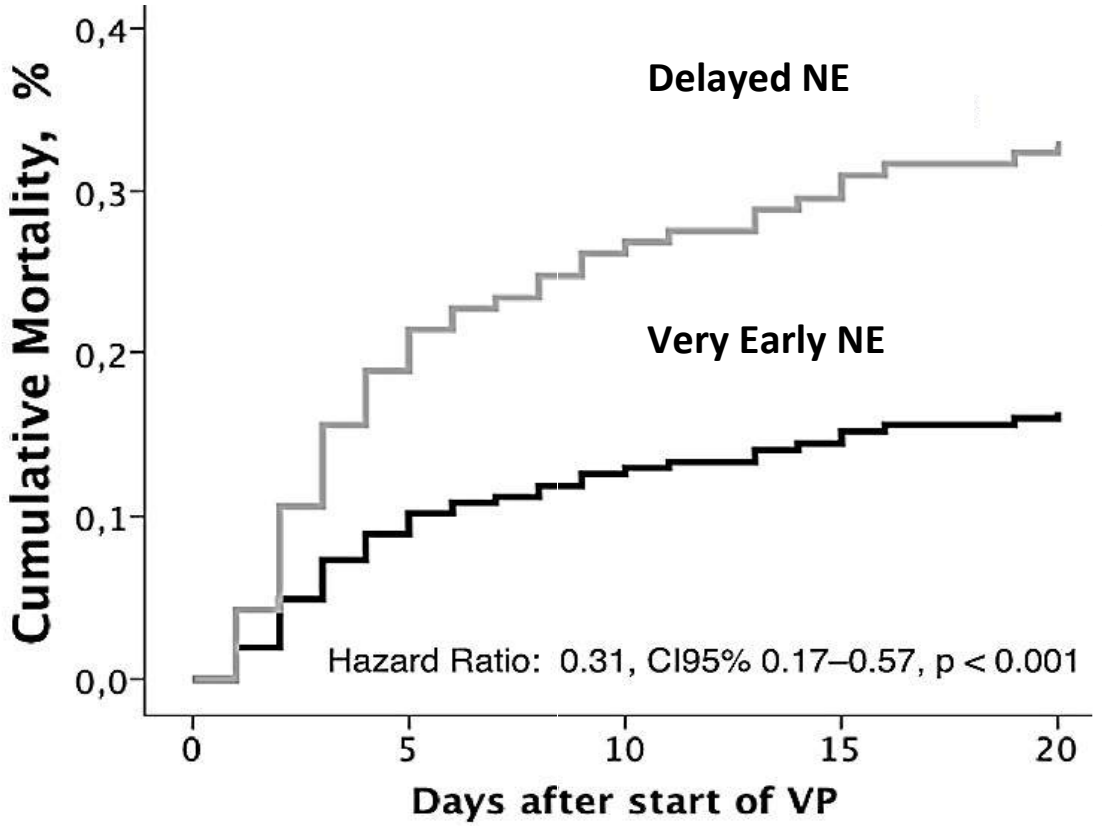
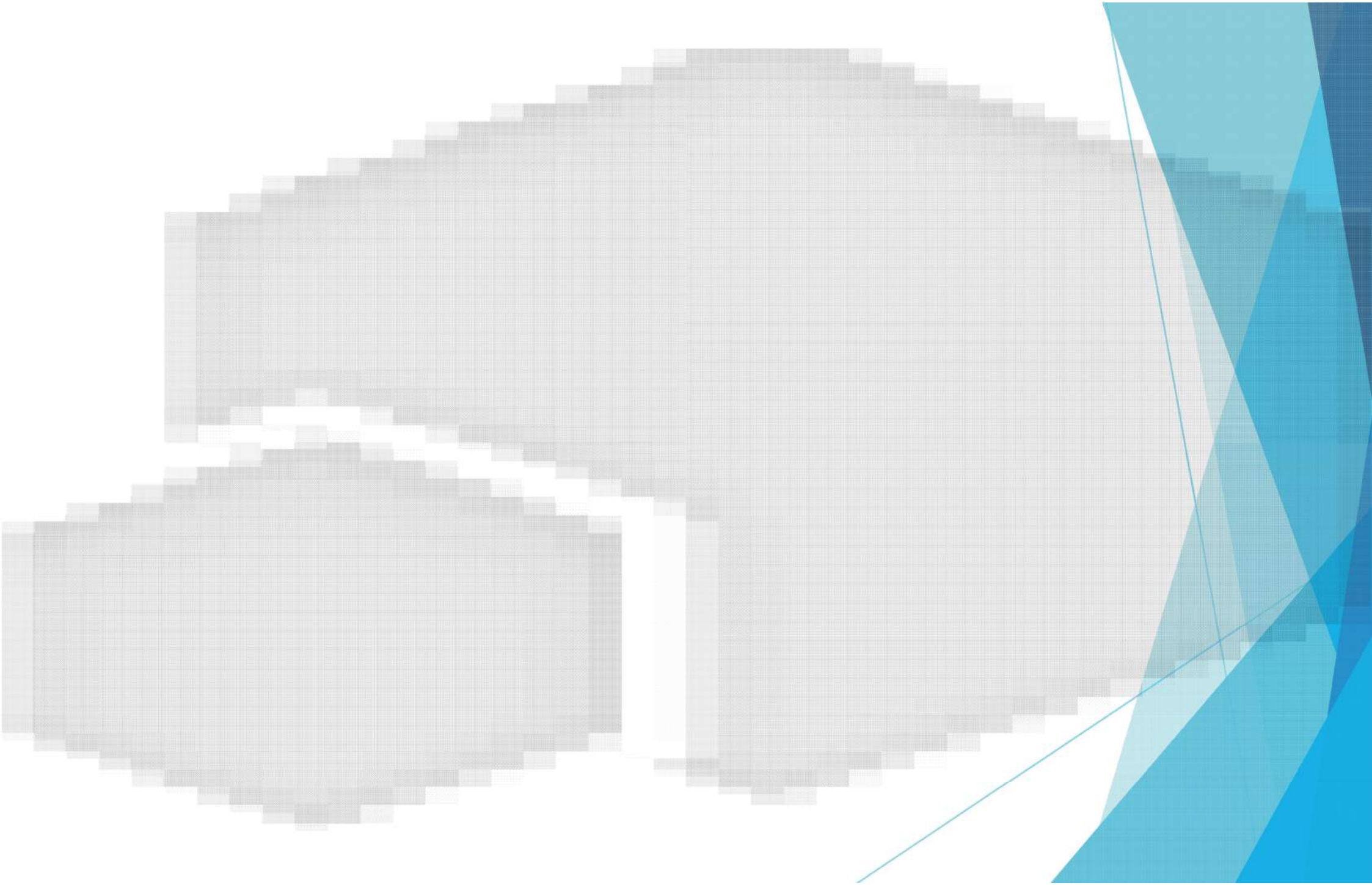
Critical Care (2020) 24:52



Intubated ventilated and worsening of respiratory state
He had 3 litres of fluids and 0.3 microgramme/Kg/min of NE

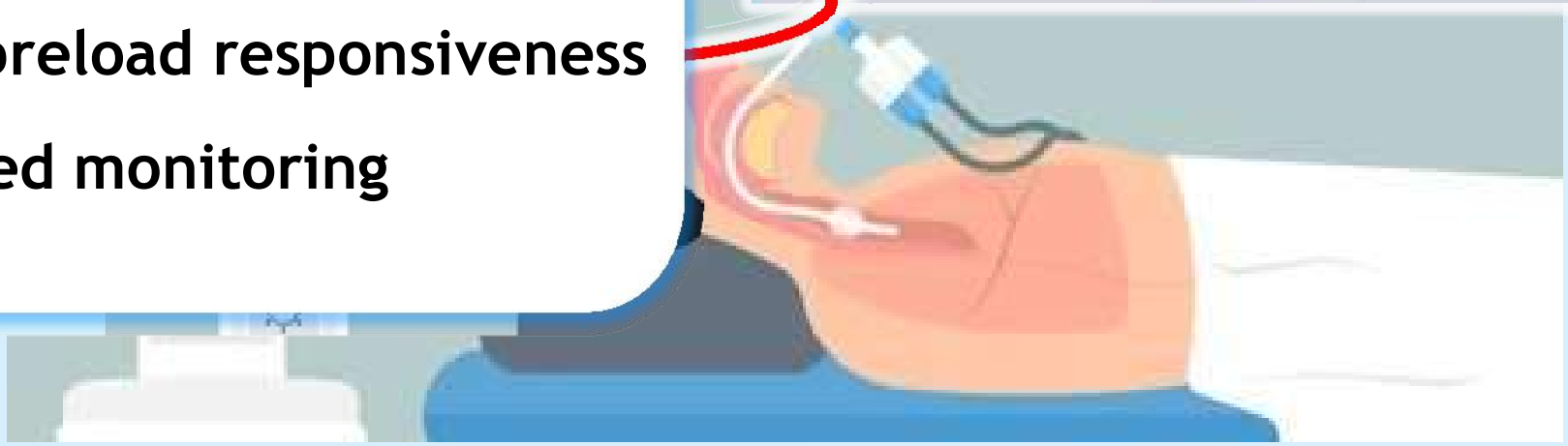
pH = 7.30
P/F: 120 mmHg
Blood lactate = 4 mmol/L



Intubated ventilated and worsening of respiratory state
He had 3 litres of fluids and 0.5 microgramme/Kg/min of NE

ttps://app.wooclap.com/events/NLIKLK/questions/667
8b2dd64ecef8db024507

. More Fluids
. Increase Norepinephrine
. Vasopressine
. Assess preload responsiveness
. Advanced monitoring



Intubated ventilated and worsening of respiratory state
He had 3 litres of fluids and 0.5 microgramme/Kg/min of NE

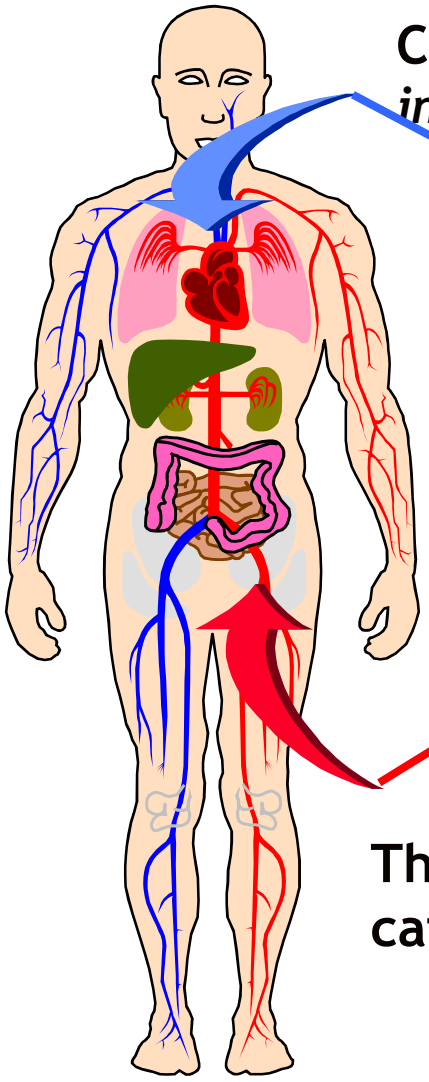
More Fluids

Increase Norepinephrine

Vasopressine

Assess preload responsiveness

Advanced monitoring



Central Venous Catheter *(cold bolus injection)*

Transpulmonary thermodilution monitor

Thermodilution femoral arterial catheter

Transpulmonary thermodilution → Intermittent cardiac output

Pulse contour analysis → Continuous cardiac output

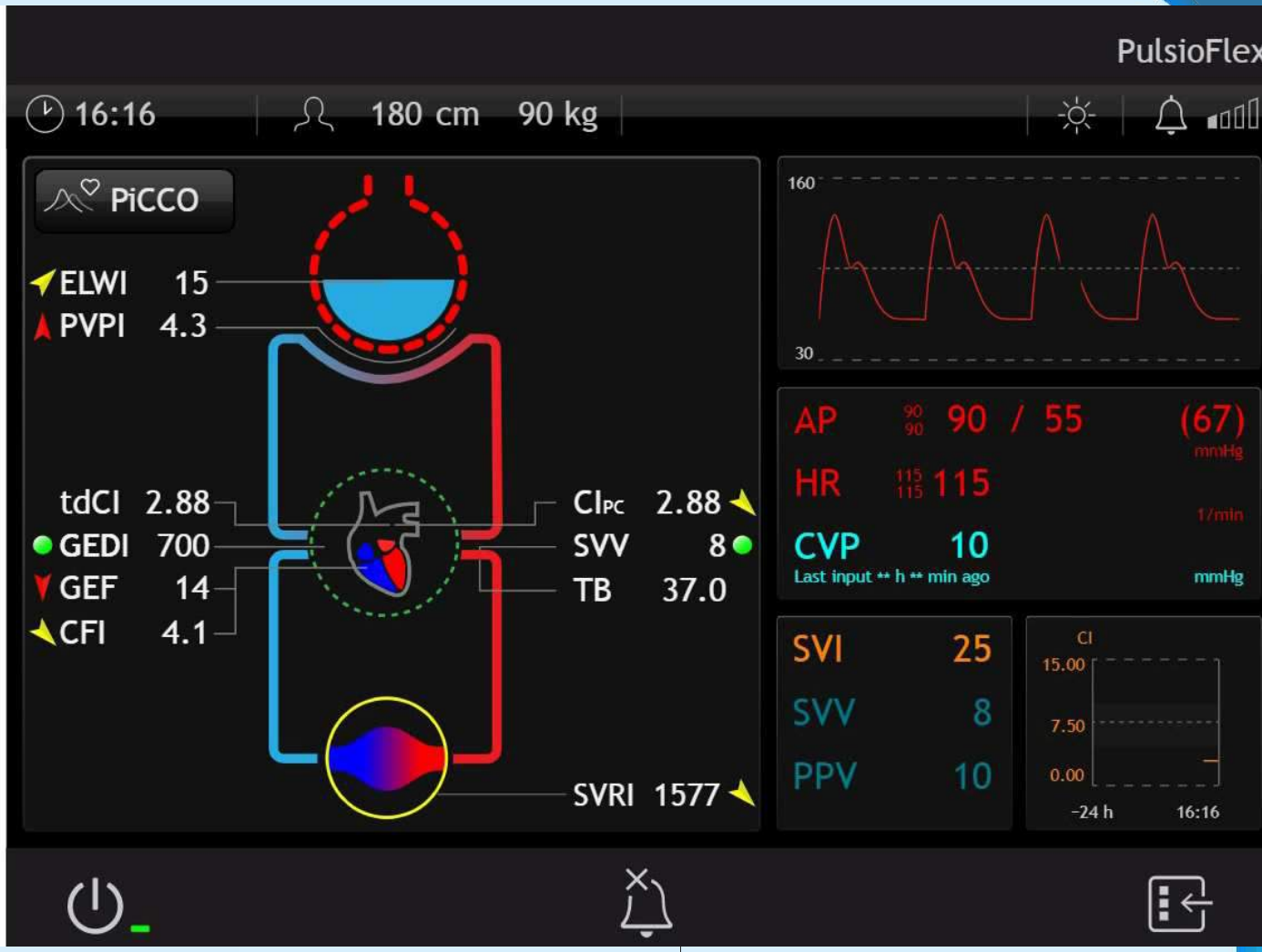
Not only

1- Global end-diastolic volume (GEDV) : → Marker of preload

2- Cardiac function index: → Index of cardiac systolic function

3- Extravascular lung water (EVLW) → quantitative measure of pulmonary edema

5- Pulmonary vascular permeability index → measure of the degree of lung capillary leak


PulsioFlex
16:16
180 cm 90 kg
PiCCO
ELWI 15
PVPI 4.3
tdCI 2.88
GEDI 700
GEF 14
CFI 4.1
CIPC 2.88
SVV 8
TB 37.0
SVRI 1577
160
30
AP 90 / 55 (67)
mmHg
HR 115
1/min
CVP 10
Last input ** h ** min ago
mmHg
SVI 25
SVV 8
PPV 10
CI
15.00
7.50
0.00
-24 h
16:16

critical care review

Predicting Fluid Responsiveness in ICU Patients*

A Critical Analysis of the Evidence

Frédéric Michard, MD, PhD; and Jean-Louis Teboul, MD, PhD

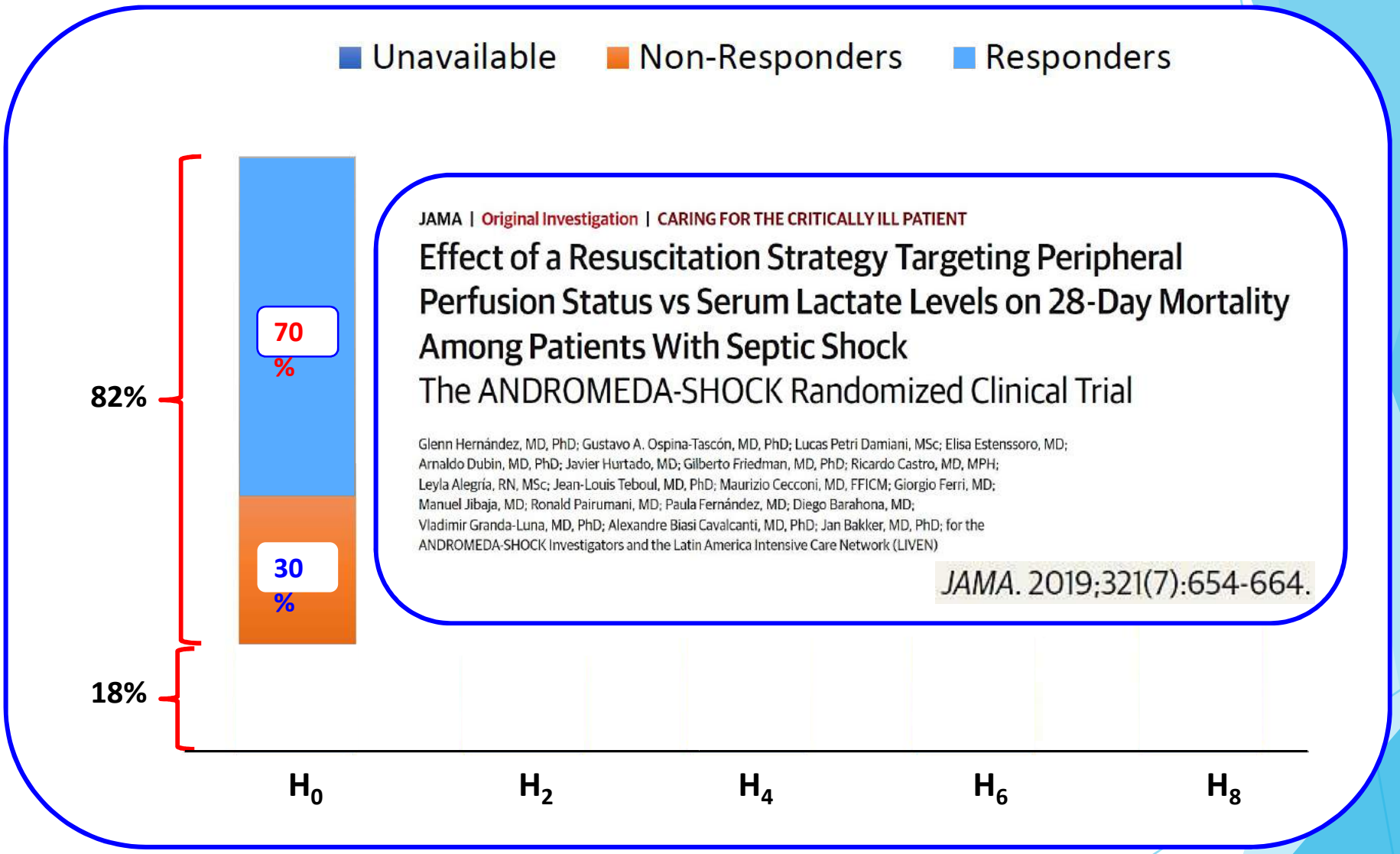
CHEST 2002; 121:2000–2008

Source	Patients, No.	FC, No.	Fluid Infused	Volume Infused, mL	Speed of FC, min	Definition of Response	Rate of Response, %
Calvin et al[2]	28	28	5% Alb	250	20–30	ΔSV > 0%	71
Schneider et al[3]	18	18	FFP	500	30	ΔSV > 0%	72
Reuse et al[4]	41	41	4.5% Alb	300	30	ΔCO > 0%	63
Magder et al[5]	33	33	9% NaCl	100–950		ΔCO > 250 mL/min	52
Di							59
Di							40
Wa							56
Tav							60
Ma							45
[illegible]							40
Michard et al[12]	40	40	HES	500	30	ΔCO > 15%	40
Feissel et al[13]	19	19	HES	8 mL/kg	30	ΔCO > 15%	53
Total	334	406					52

Only **52%** of patients **increase** their **cardiac output** in response to **fluid** administration

Why do we need to predict fluid responsiveness?

- Not all the patients are fluid responsive
- Fluid responsiveness is a dynamic phenomenon



JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

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

Glenn Hernández, MD, PhD; Gustavo A. Ospina-Tascón, MD, PhD; Lucas Petri Damiani, MSc; Elisa Estenssoro, MD; Arnaldo Dubin, MD, PhD; Javier Hurtado, MD; Gilberto Friedman, MD, PhD; Ricardo Castro, MD, MPH; Leyla Alegría, RN, MSc; Jean-Louis Teboul, MD, PhD; Maurizio Cecconi, MD, FFICM; Giorgio Ferri, MD; Manuel Jibaja, MD; Ronald Pairumani, MD; Paula Fernández, MD; Diego Barahona, MD; Vladimir Granda-Luna, MD, PhD; Alexandre Biasi Cavalcanti, MD, PhD; Jan Bakker, MD, PhD; for the ANDROMEDA-SHOCK Investigators and the Latin America Intensive Care Network (LIVEN)

JAMA. 2019;321(7):654-664.

Hernandez et al. *JAMA* 2019

Why do we need to predict fluid responsiveness?

- Not all the patients are fluid responsive
- Fluid responsiveness is a dynamic phenomenon
- Fluid overload is harmful

Sepsis in European intensive care units: Results of the SOAP study*

Jean-Louis Vincent, MD, PhD, FCCM; Yasser Sakr, MB, BCh, MSc; Charles L. Sprung, MD; V. Marco Ranieri, MD; Konrad Reinhart, MD, PhD; Herwig Gerlach, MD, PhD; Rui Moreno, MD, PhD; Jean Carlet, MD, PhD; Jean-Roger Le Gall, MD; Didier Payen, MD; on behalf of the Sepsis Occurrence in Acutely Ill Patients Investigators

Crit Care Med 2006; 34:344–353

Table 7. Multivariate, forward stepwise logistic regression analysis in sepsis patients (n = 1177), with intensive care unit mortality as the dependent factor

	OR (95% CI)	*p* Value
SAPS II score[a] (per point increase)	1.0 (1.0–1.1)	<.001
Cumulative fluid balance[b] (per liter increase)	1.1 (1.0–1.1)	.001
Age (per year increase)	1.0 (1.0–1.0)	.001
Female gender	1.4 (1.0–1.8)	.044

During sepsis: positive cumulative fluid balance is an independent factor associated with mortality

Why do we need to predict fluid responsiveness?

- Not all the patients are fluid responsive
- Fluid responsiveness is a dynamic phenomenon
- Fluid overload is harmful
- Use of **fluid responsiveness** tests is associated with improved **outcome**

Characteristics of resuscitation, and association between use of dynamic tests of fluid responsiveness and outcomes in septic patients: results of a multicenter prospective cohort study in Argentina

Arnaldo Dubin[1*], Cecilia Loudet[2], Vanina S. Kanoore Edul[3], Javier Osatnik[4], Fernando Ríos[5], Daniela Vásquez[6], Mario Pozo[7], Bernardo Lattanzio[8], Fernando Pálizas[7], Francisco Klein[9], Damián Piezny[5], Paolo N. Rubatto Birri[1], Graciela Tuhay[9], Analía García[10], Analía Santamaría[11], Graciela Zakalik[12], Cecilia González[13] and Elisa Estenssoro[2] on behalf of the Investigators of the SATISEPSIS group

Ann. Intensive Care (2020) 10:40

- **National, multicenter prospective cohort study** (n = 787) fulfilling **Sepsis-3 definitions**
- Examine **the association** between the **use of dynamic tests** of fluid responsiveness and **outcome**

Only 584 patients received fluids

Table 4 Independent determinants of mortality according to logistic regression analysis

Variable	Odds ratio	[CI 95%]	*P*
Charlson score	1.21	[1.07–1.36]	0.002
SOFA score	1.16	[1.07–1.26]	< 0.0001
Serum lactate	1.21	[1.08–1.37]	0.001
Mechanical ventilation	12.2	[5.73–26.00]	< 0.0001
Dynamic tests of fluid responsiveness	0.37	[0.21–0.67]	0.001

EDITORIAL Open Access

Equilibrating SSC guidelines with individualized care

Jean-Louis Vincent[1*], Mervyn Singer[2], Sharon Einav[3], Rui Moreno[4], Julia Wendon[5], Jean-Louis Teboul[6], Jan Bakker[7,8,9,10], Glenn Hernandez[11], Djillali Annane[12], Angélique M. E. de Man[13], Xavier Monnet[14], V. Marco Ranieri[15], Olfa Hamzaoui[16], Jukka Takala[17], Nicole Juffermans[18,19], Jean-Daniel Chiche[20], Sheila N. Myatra[21] and Daniel De Backer[22]

Critical Care (2021) 25:397

2 Initial resuscitation

We recommend **individualizing** initial fluid resuscitation. No single formula can be applied to all patients, as **fluid requirements vary** substantially (depending on the source of sepsis and preexis cardiovascular function).

We recommend **individualizing** fluid therapy using **dynamic challenges.**

GUIDELINES

Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021

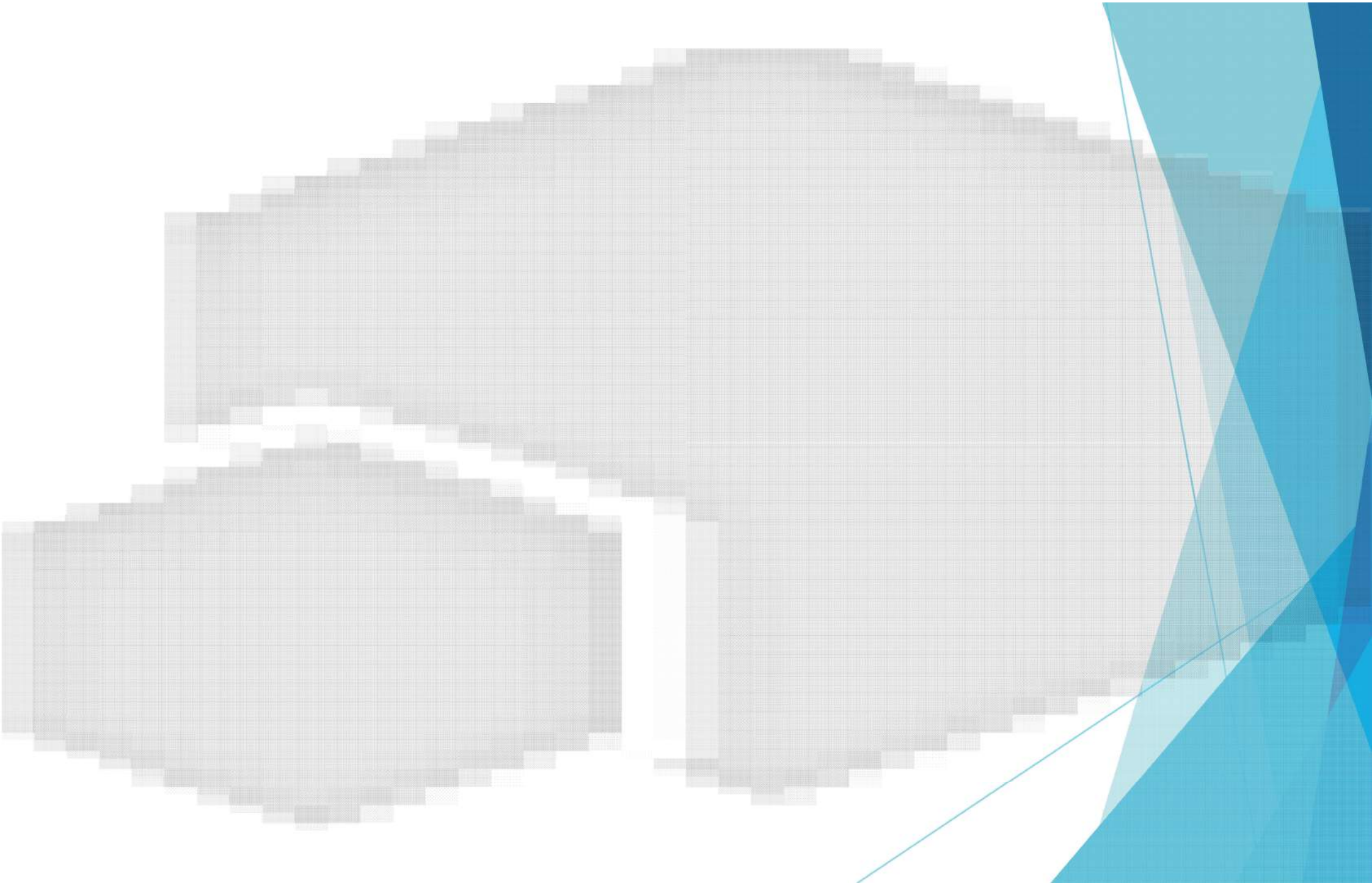
Intensive Care Med (2021) 47:1181–1247

. For adults with sepsis or septic shock, we **suggest** using dynamic measures to guide fluid resuscitation, over physical examination or static parameters alone

Veak recommendation, very low-quality evidence

Remarks

Dynamic parameters include response to a passive leg raise or a fluid bolus, using stroke volume (SV), stroke volume variation (SVV), pulse pressure variation (PPV), or echocardiography, where available



How can I assess preload responsiveness ?

https://app.wooclap.com/events/NLIKLK/questions/66748cb98233377c96daa4ac

1. Using PPV
2. Using SVV
3. Passive leg raising
4. Inferior Vena cava variation

How can I assess preload responsiveness ?

1. **Using PPV**
2. **Using SVV**
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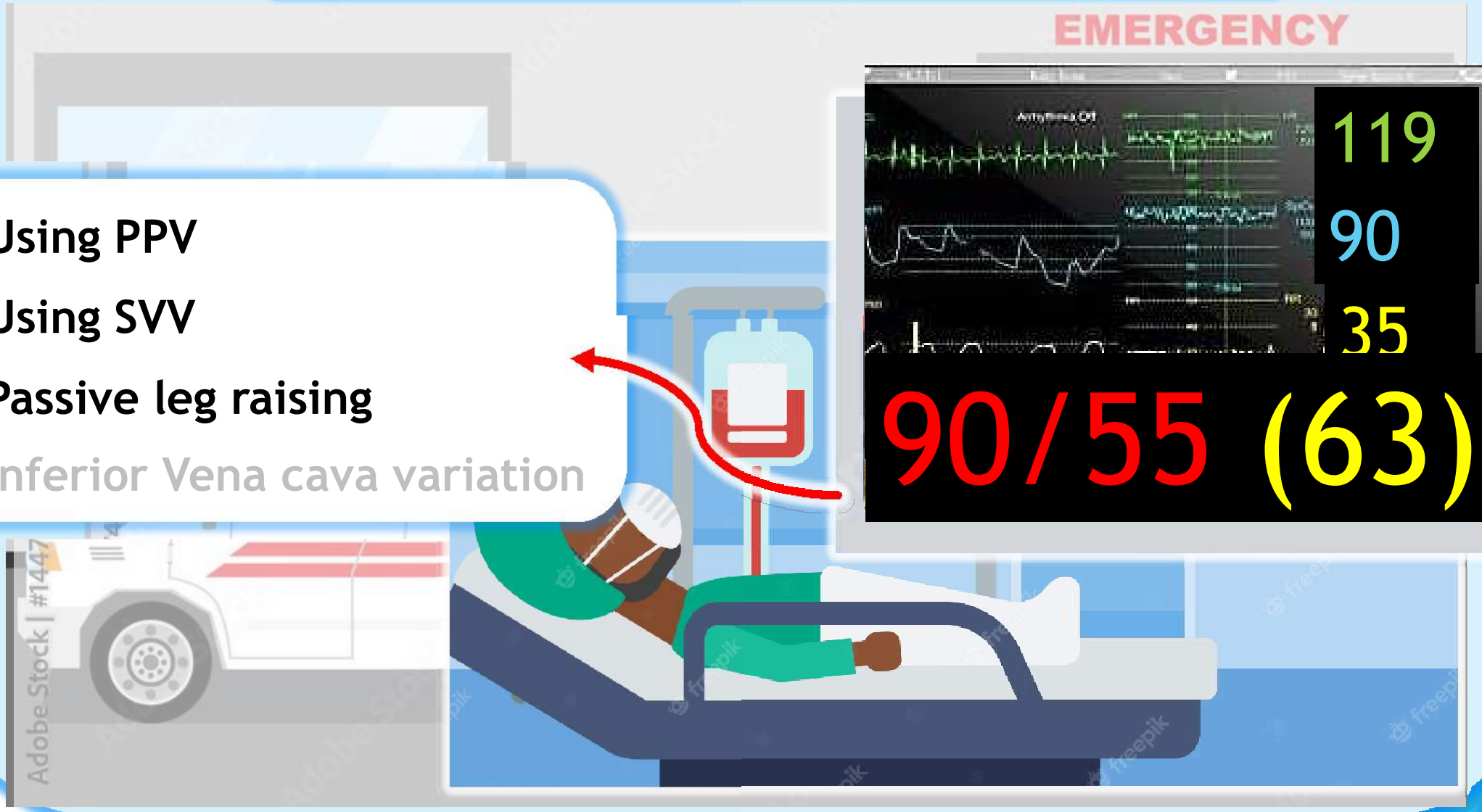
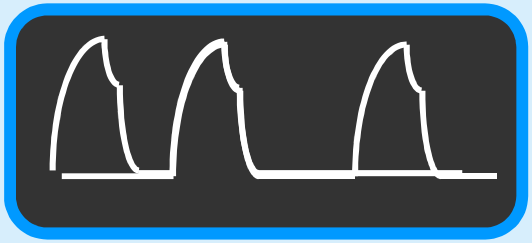
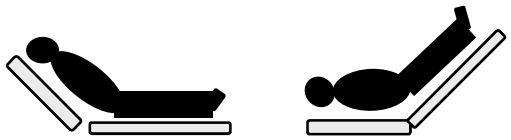
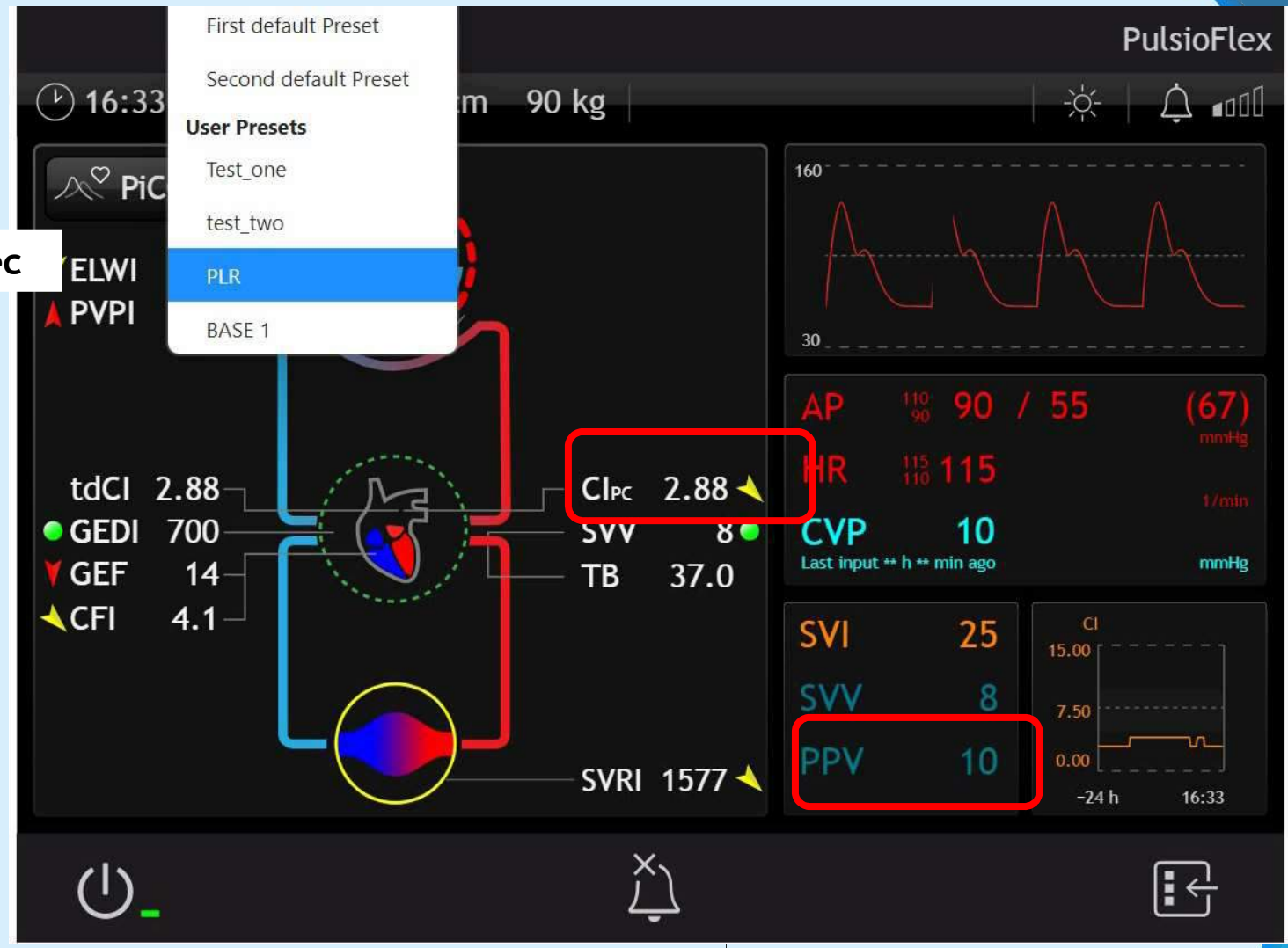


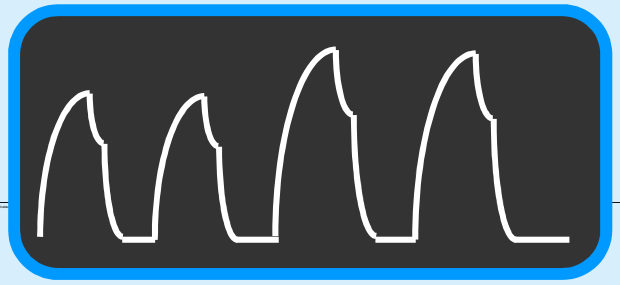


End-expiratory occlusion for 15 sec

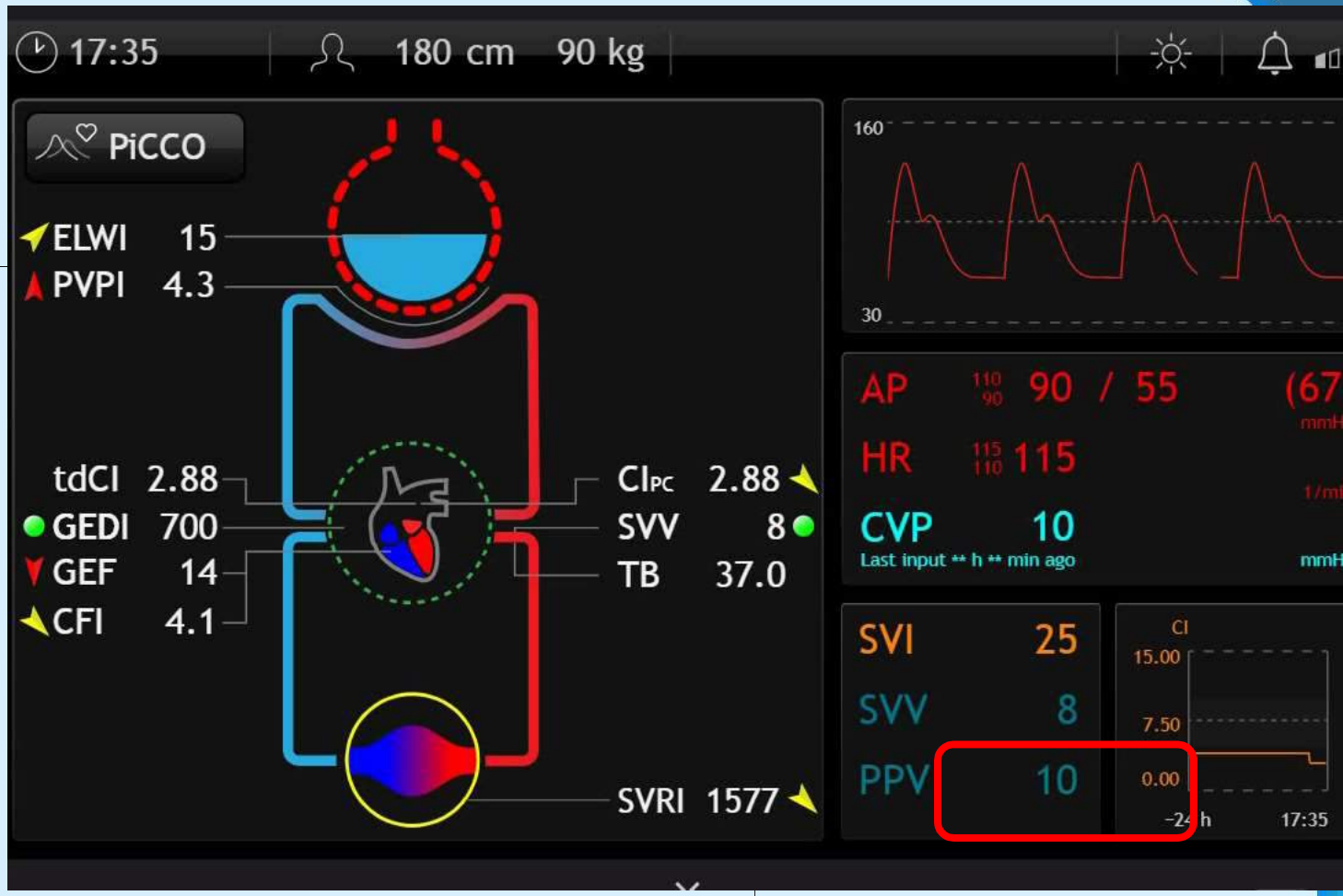


PLR





Tidal volume challenge
for 1 minute



Transpulmonary thermodilution:

Useful to **guide** fluids

In particular in patients with **shock** and **ARDS**

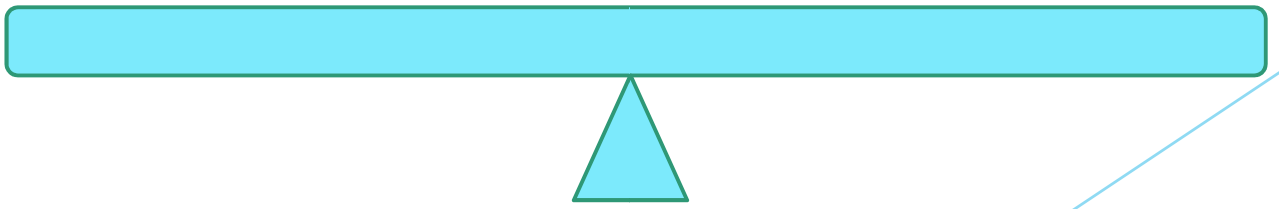
benefit/risk balance

Prediction of **fluid responsiveness**

- **PPV** and **SVV**
- **Response** of **CO** (real time) **to PLR test**

Evaluation of the **tolerance to fluids**

- **EVLWi**
- **PVPI**



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- **EVLWi**
- **PVPI**

⟹ **decision**

- To begin
- To continue
- To stop

fluids

creatinine = 250 µmol/L

Na^+ = 140 mmol/L

K^+ = 4 mmol/L

ALT = 2,500 IU/L

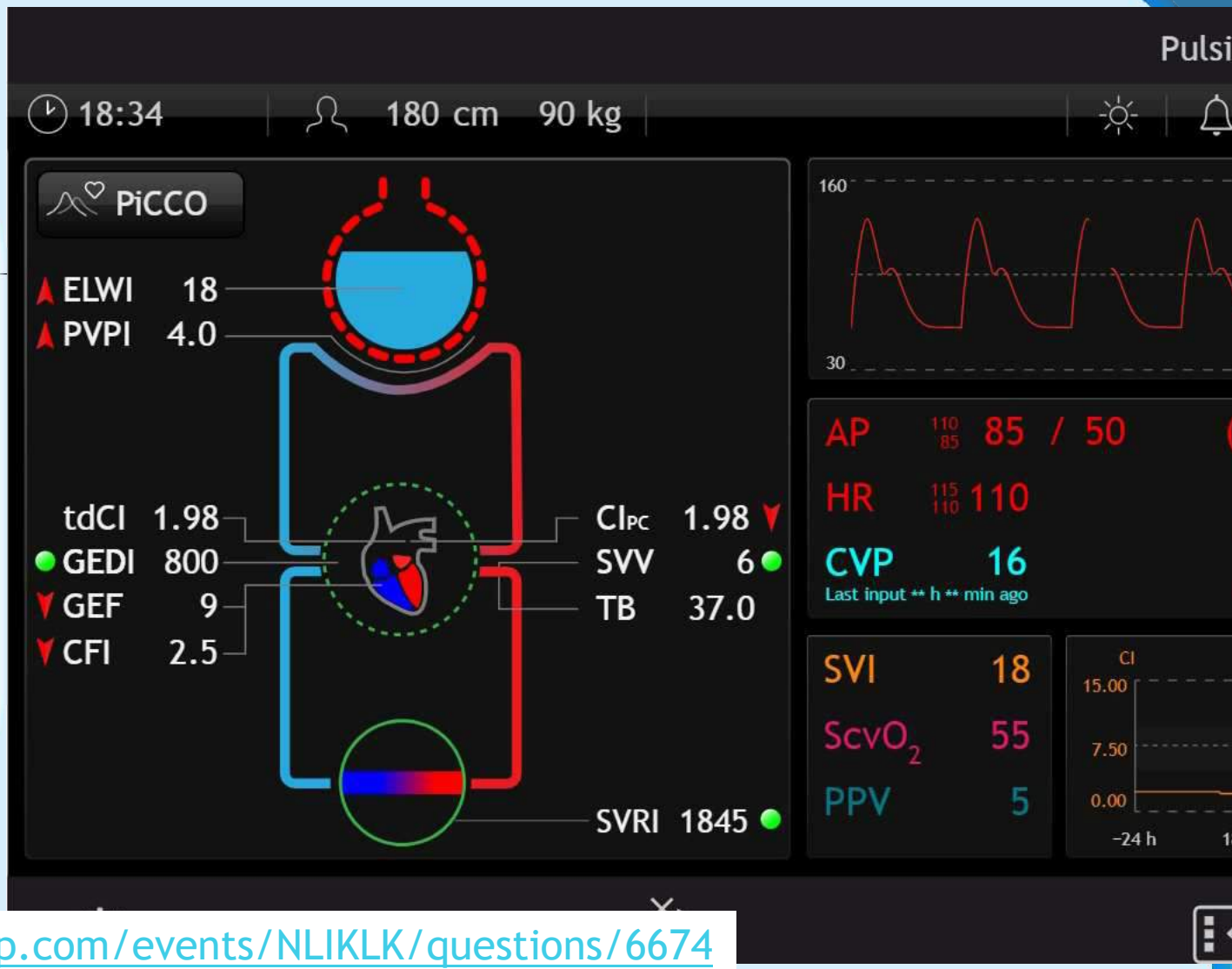
AST = 3,500 UI/L

pH = 7.10

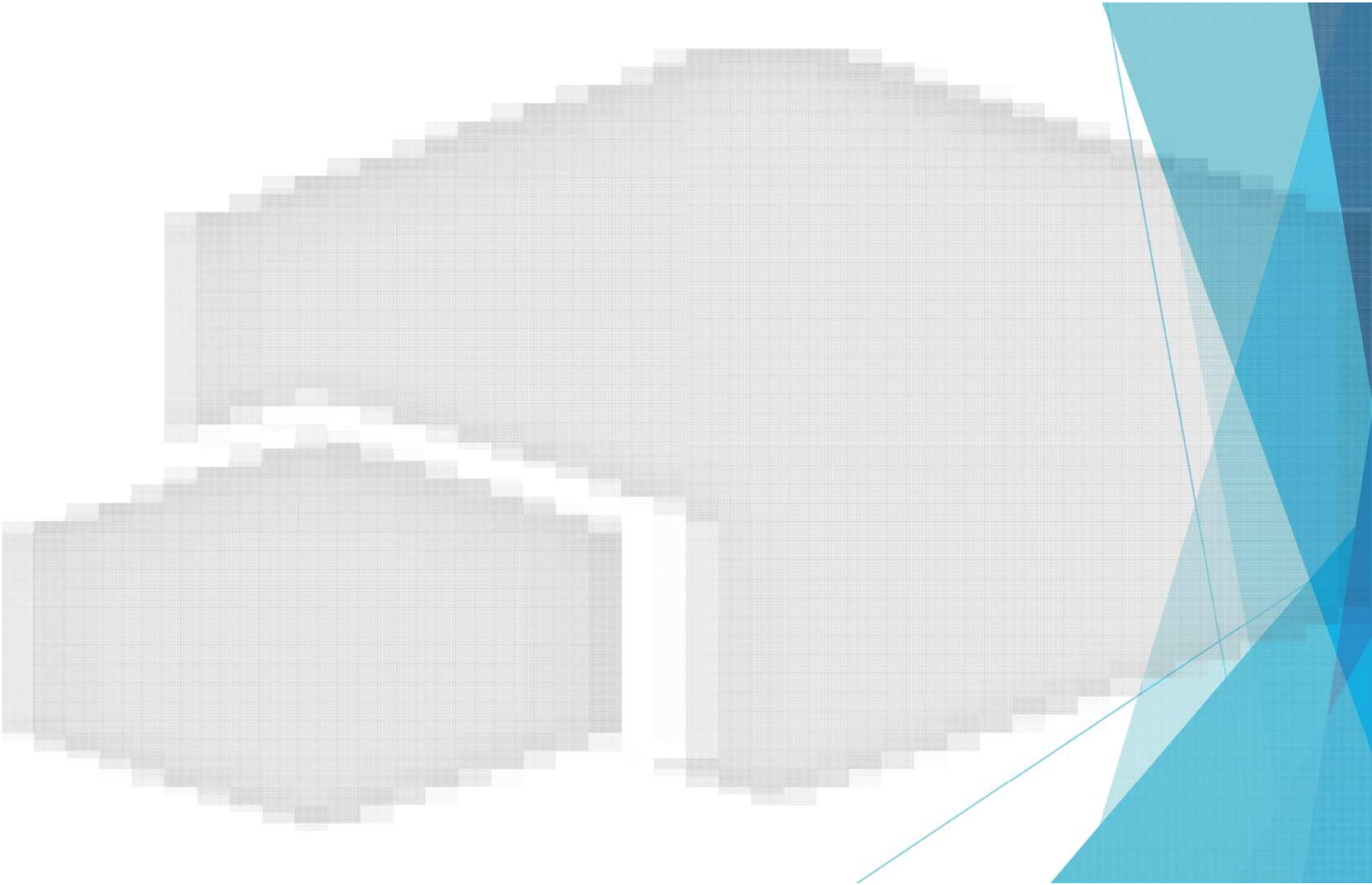
PaO_2 = 95 mmHg

$PaCO_2$ = 40 mmHg

Blood lactate = 10 mmol/L



https://app.wooclap.com/events/NLIKLK/questions/66748e5fe671de41113b70eb



Renal failure

creatinine = 250 µmol/L

Na^+ = 140 mmol/l

Liver failure

K^+ = 4 r

ALT = 2,500 IU/L

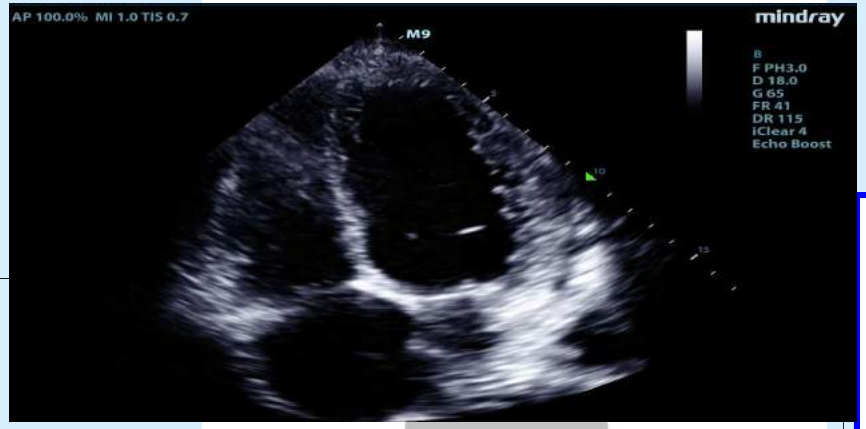
AST = 3,500 UI/L

pH = 7.10

PaO_2 = 95 mmHg

$PaCO_2$ = 40 mmHg

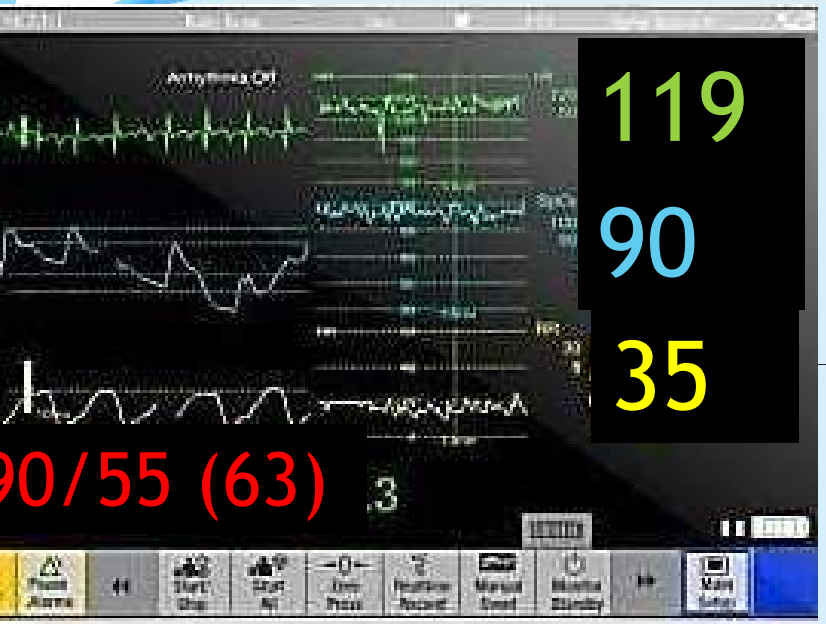
Blood lactate = 10 mmol/L

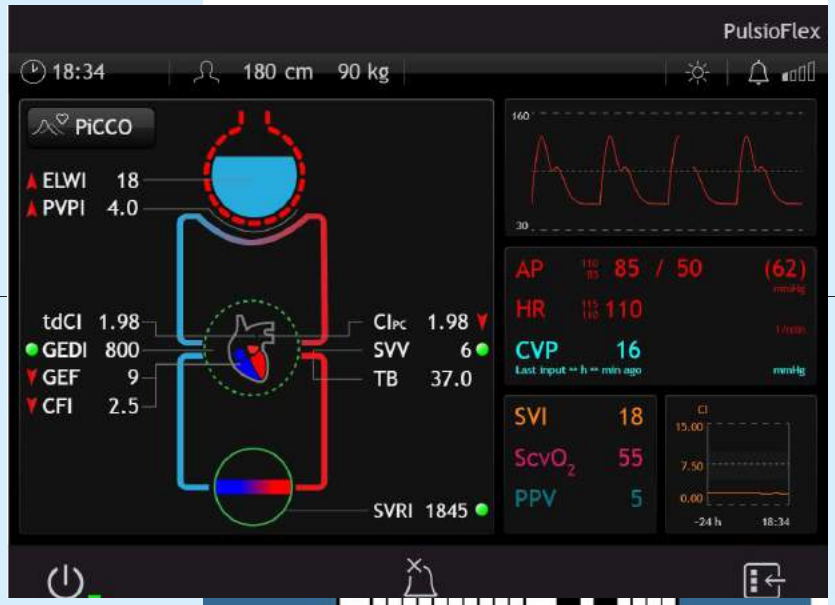


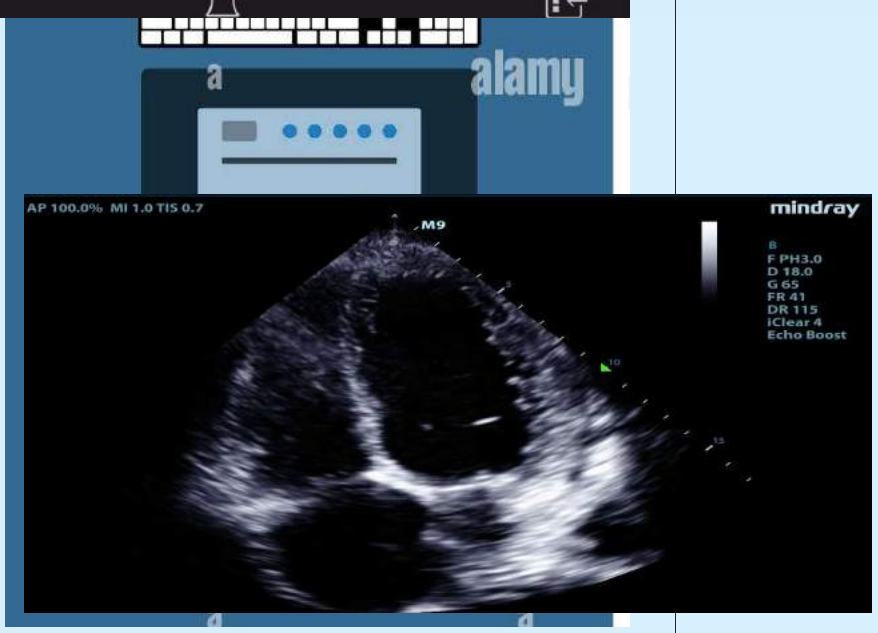
Transthoracic echocardiography

Left Ventricular EF	**20%**
Velocity-Time Integral	**9 cm**
sPAP	**30 mmHg**
Right Ventricle	**Normal**

- SARS-CoV-2 related **myocarditis**
- Inotropic Treatment: **dobutamine**


119
90
35
90/55 (63)


PulsioFlex
18:34
180 cm 90 kg
PiCCO
ELWI 18
PVPI 4.0
tdCI 1.98
GEDI 800
GEF 9
CFI 2.5
CIPC 1.98
SVV 6
TB 37.0
SVRI 1845
AP 85 / 50 (62)
HR 110
CVP 16
SVI 18
ScvO2 55
PPV 5


AP 100.0% MI 1.0 TIS 0.7
M9
mindray
F PH3.0
D 18.0
G 65
FR 41
DR 115
iClear 4
Echo Boost