65 or Not?

What Is the Target for Septic Shock — MAP or Others?

馬偕紀念醫院 淡水內科加護病房 趙文綺

2026-8-2 台灣胸腔暨重症加護醫學會 115年北區重症聯甄課程

馬偕紀念醫院 MacKay Memorial Hospital

CASE · 03:00

This Patient Is “Resuscitated.” Now What?

68 M · pneumonia, septic shock

Crystalloid 30 mL/kg · NE 0.30 μg/kg/min
HR 112　CVP 11　UO 0.4 mL/kg/hr
Lactate 4.2 mmol/L（入院 4.6）
Mottling score 3 · source control 進行中

68
mmHg
MAP

74
%
$ScvO_2$

5.0
sec
CRT
Abnormal

8.5
mmHg
$Pv\text{-}aCO_2$
Abnormal

By the 2001 Rivers bundle, this patient is fully resuscitated.
數字全部達標，那你現在要做什麼？

Your Next Move?

1

Give another 500 mL

「CVP 才 11，還有空間」

2

Push MAP to 80–85

「灌流壓不夠才會 lactate 高」

3

Add nothing — reassess

「數字達標，問題不在壓力」

All three are defensible on today's evidence.
重點不在選哪一個，而在你憑什麼決定。

PART I · MARCH 2026

The SSC 2026 Guideline

01

Mean arterial pressure

MAP 65 over higher targets

STRONG, Certainty moderate。
實務上無法維持在正好 65，以 ±5 mmHg 的區間 titrate。

02

NEW · aged 65 or older

Initial MAP range 60–65 mmHg

Conditional，certainty low。
2021 版沒有這一條， The 65 trial

03

NEW · after the acute phase

Active fluid removal | CRT as adjunct

急性復甦期後建議主動移除液體
CRT 仍列為灌流輔助指標。

指引已經給了下限，但MAP 達標之後要看什麼？

Prescott HC, et al. Surviving Sepsis Campaign 2026. Crit Care Med / Intensive Care Med, 23 March 2026

I

Shock and the Meaning of MAP 65

休克的本質與 MAP 65 的定位

PART I · ORIGIN

Where Did the Number 65 Come From?

01

Physiology

Autoregulation plateau ≈ 60–70 mmHg

腦與腎的自我調節平台下緣，族群平均值。

02

Rivers 2001 EGDT

MAP 65 entered inside a bundle

從未被單獨做過 dose-finding

03

Re-examined, unchanged

SSC 2026 keeps 65 as the initial target

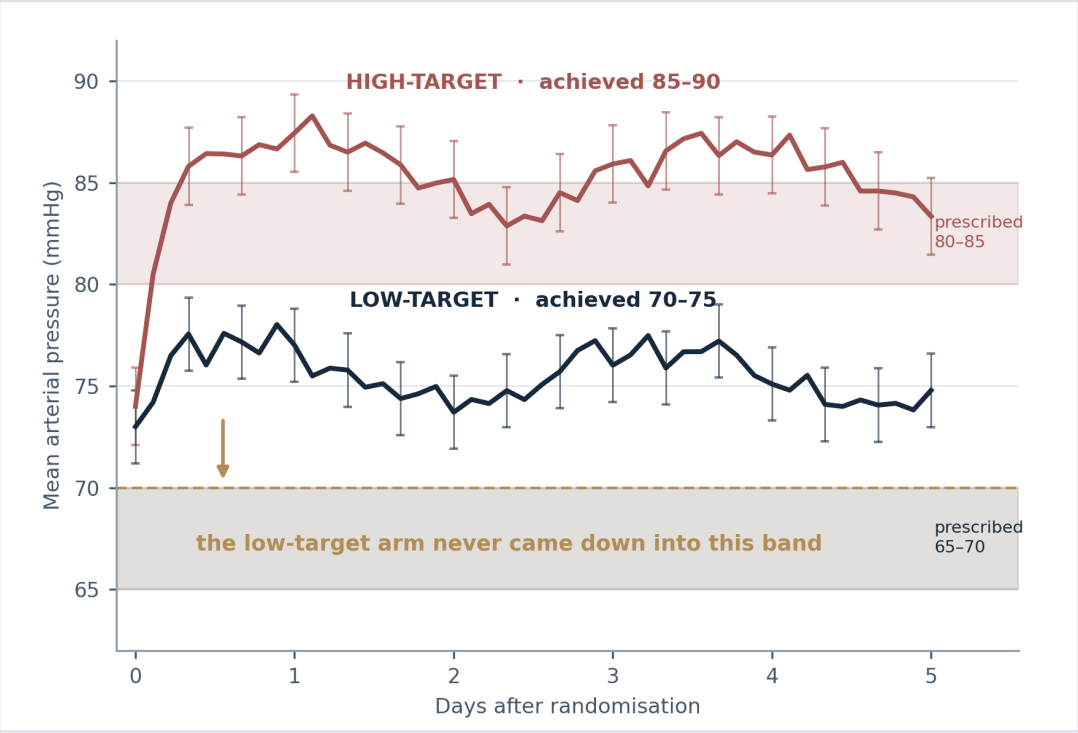
支持它的是「更高沒有更好」，不是「65 剛剛好」。

MAP 65 是 bundle 的一部分，證據等級不等於被單獨驗證過。

SEPSISPAM — And the Low Arm Was Never at 65

STUDY POPULATION

n = 776 analysed · 29 French centres · septic shock refractory to fluid resuscitation · mean age 65 · chronic hypertension 43–45%（隨機分派時的分層變項）· MAP 80–85 vs 65–70 held up to 5 days



Redrawn from Asfar P, et al. N Engl J Med 2014;370:1583–1593, Figure 2.

43.8 / 42.3

90-day mortality (%)

high vs low

HR 1.04 (0.83–1.30)　p = .74

70–75

Achieved MAP in the low arm (mmHg)　兩組實際 MAP 都高於處方區間：65 從未被真正測試過

THE ONLY SIGNAL

Kidneys, in chronic hypertension only

RRT d1–7　31.7 vs 42.2%

Creatinine×2　38.9 vs 52.0%

both p < .05

THE PRICE

New atrial fibrillation

6.7 vs 2.8% · p = .02

升壓劑輸注 4.7 vs 3.7 天

Higher MAP did not improve survival and increased the risk of atrial arrhythmia

Asfar P, et al. SEPSISPAM. N Engl J Med 2014;370:1583–1593 ·

PART I · 2020 THE FLOOR

The 65 Trial — Can You Go Below 65?

STUDY POPULATION

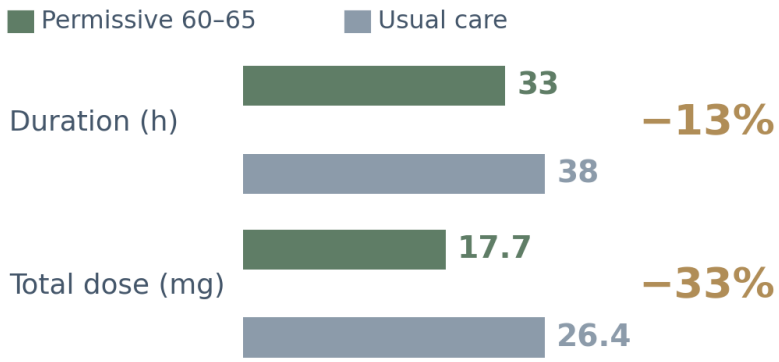
n ≈ 2600 · 65 UK ICU · aged ≥ 65 · vasodilatory hypotension already on vasopressors · Permissive hypotension (MAP 60–65) vs usual care · chronic hypertension ≈ 46% · mean age ≈ 75

41.0 / 43.8

90-day mortality (%)

permissive vs usual, ARD −2.85 (95% CI −6.75 to 1.05), p = .15

WHAT IT ACTUALLY DELIVERED
JAMA 2020, TABLE 2 (MEDIANS)



WHAT IT ESTABLISHES

Going lower is safe in the elderly

死亡率沒有增加，而升壓劑暴露顯著下降。

這是唯一支持「降階安全」的大型試驗 (RCT)。

Permissive hypotension safely reduced vasopressor exposure in the elderly without significantly increasing mortality, challenging the necessity of rigid higher targets.

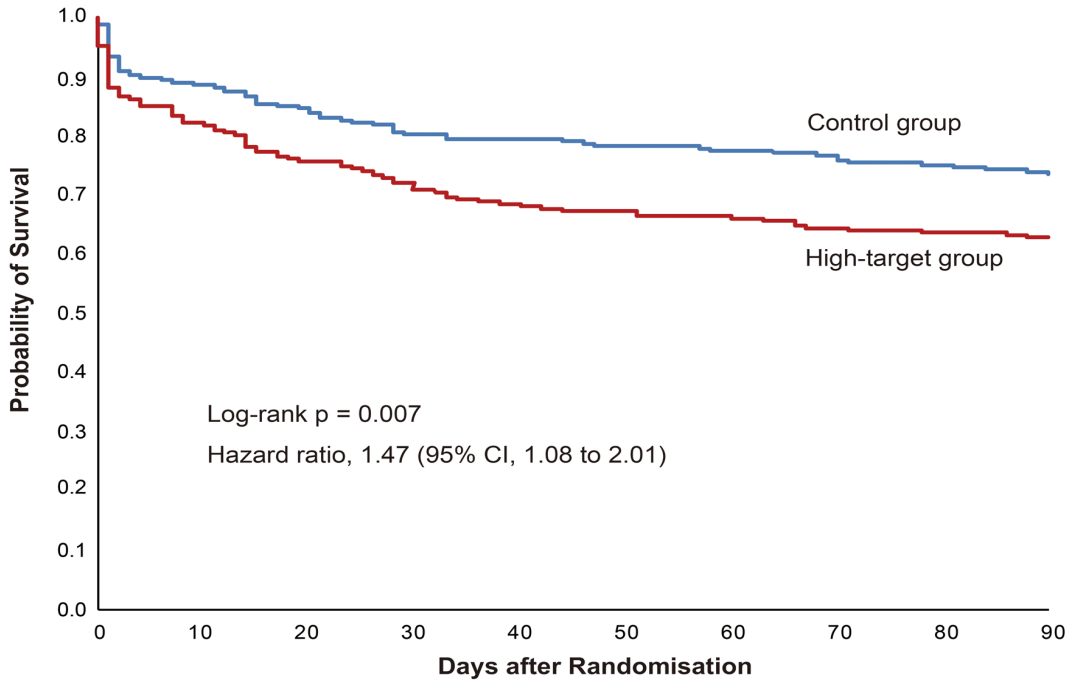
Lamontagne F, et al. The 65 Trial. JAMA 2020;323:938–949

PART I · 2025

OPTPRESS — High MAP Is Not Just Useless, It Harms

STUDY POPULATION

n = 516 · 29 Japanese centres · septic shock aged ≥65 · median age 78 (73–85) · Chronic hypertension 53% · median SOFA 10 / APACHE II 27 · MAP 80–85 vs 65–70 held for 72 h



No. at Risk

Control group	259	224	212	203	200	198	195	193	189	186
High-target group	257	204	188	179	170	168	165	161	158	156

39.3 / 28.6

90-day mortality (%) high vs control

Risk difference +10.7 (2.6–18.9), HR 1.47 (1.08–2.01), log-rank p = .007

EVERY ENDPOINT AGREES

Secondary outcomes point the same way

28-day death 30.4 vs 21.6%
Sepsis death 30.0 vs 17.8%
Vent-free 15 vs 18 d
RRT-free 18 vs 20 d

TWO DETAILS

Stopped early for harm

即使用早期 vasopressin 的 catecholamine-sparing protocol 也擋不住。

慢性高血壓次族群同樣無獲益。

Endo A, et al. OPTPRESS. Intensive Care Med 2025;51:883–892.

Chronic Hypertension — Three Directions

Higher MAP spared the kidneys

SEPSISPAM 2014 · n = 76

慢性高血壓 44%（分層變項）
RRT　31.7 vs 42.2%
Cr ×2　38.9 vs 52.0%
交互作用 p = .04 / .009

Lower MAP looked better

The 65 Trial 2020 · n ≈ 2600

慢性高血壓 46%
90-d death　38.2 vs 44.3%
adjusted OR 0.67　p int .047
無高血壓者　43.3 vs 43.4%

Higher HAP No benefit — net harm

OPTPRESS 2025 · n = 516

慢性高血壓 53%
次族群無獲益
整體 39.3 vs 28.6%　HR 1.47
因傷害提前中止

Three Trials, Three Answers.

The 2020 signal also vanishes on the risk-ratio scale (p .047 → .12).
不要因為「有高血壓」就把MAP目標訂高。

Asfar 2014 Table 2 · Lamontagne 2020 Figure 3 · Endo 2025　（SEPSISPAM 以慢性高血壓分層隨機；另兩者為預先指定次族群）三者皆未調整多重比較。

PART I · EVIDENCE

Four RCTs That Tested MAP High vs. Low

Trial	Design	Result
SEPSISPAM NEJM 2014 · n=776	MAP 80–85 vs 65–70	死亡率無差異；慢性高血壓次族群 RRT↓，但心房顫動↑。
The 65 Trial JAMA 2020 · n≈2600	≥65y：60–65 vs usual care	90 天死亡率無差異；升壓劑暴露顯著減少。
OPTPRESS ICM 2025 · n=516	≥65y：80–85 vs 65–70，72 小時	死亡率 39.3% vs 28.6%，因傷害提前中止；無任何次族群獲益。
ANDROMEDA-SHOCK-2 JAMA 2025	80–85 僅作 1 小時可逆 test	約 50% 因此 CRT 正常化；沒反應就調回。

2014 更高沒有更好 → 2020 更少反而可以 → 2025 更高會傷人。

Asfar 2014 · Lamontagne 2020 · Endo 2025 · Hernández 2019/2025.

PART I · WHY MAP IS NOT ENOUGH, NOT A THEORY

What Do 1467 “MAP On-Target” Patients Look Like?

ANDROMEDA-SHOCK-2 baseline · n = 1467 · 86 ICUs / 19 countries · median age 66 · APACHE II 19 · 100% on norepinephrine · median MAP 69 mmHg — all on target

58–62%

CRT > 3 sec

51–52%

Pv-aCO_2 > 6 mmHg

73–74%

$ScvO_2$ (normal)

3.6–3.7

Lactate mmol/L

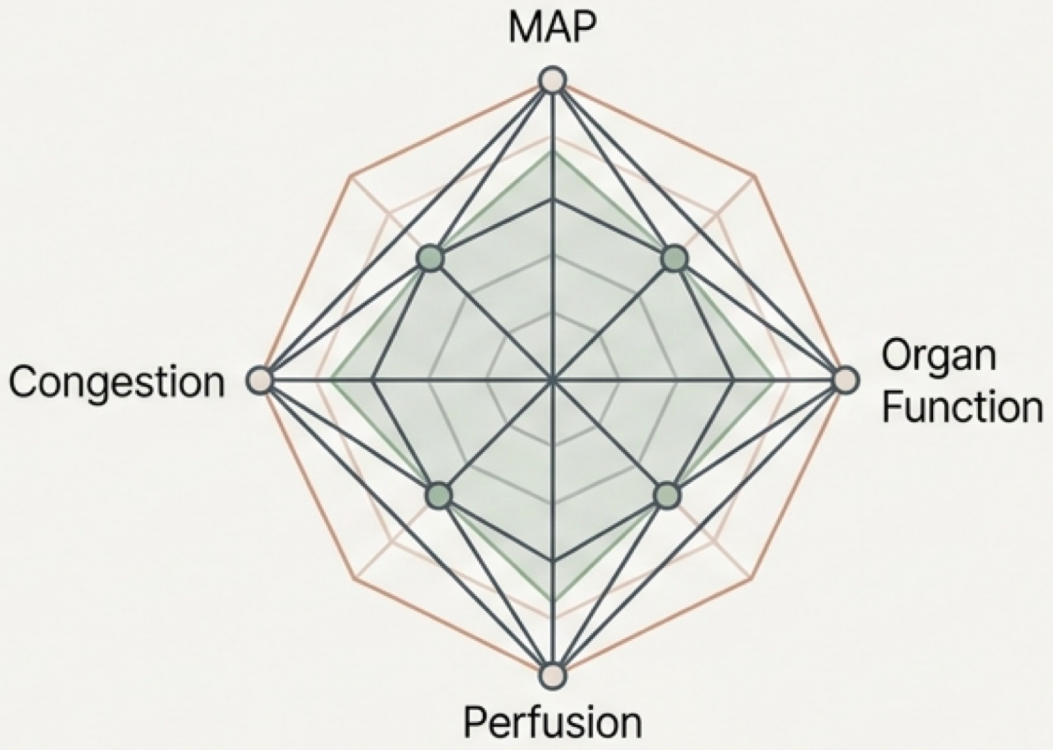
On-target pressure proves nothing about perfusion.

這不是罕見情境，這是 septic shock 的常態。

ANDROMEDA-SHOCK-2, JAMA 2025;334:1988

The Reality of Hemodynamic Incoherence

The Outdated Paradigm:
Chasing a single numerical threshold.



The 2026 Paradigm:
Multimodal optimization.

MAP 65 mmHg is a starting floor, not a universal resuscitation endpoint.
The true target is restoring effective organ perfusion at the lowest treatment cost.

Microcirculatory and Mitochondrial Distress Syndrome (MMDS)

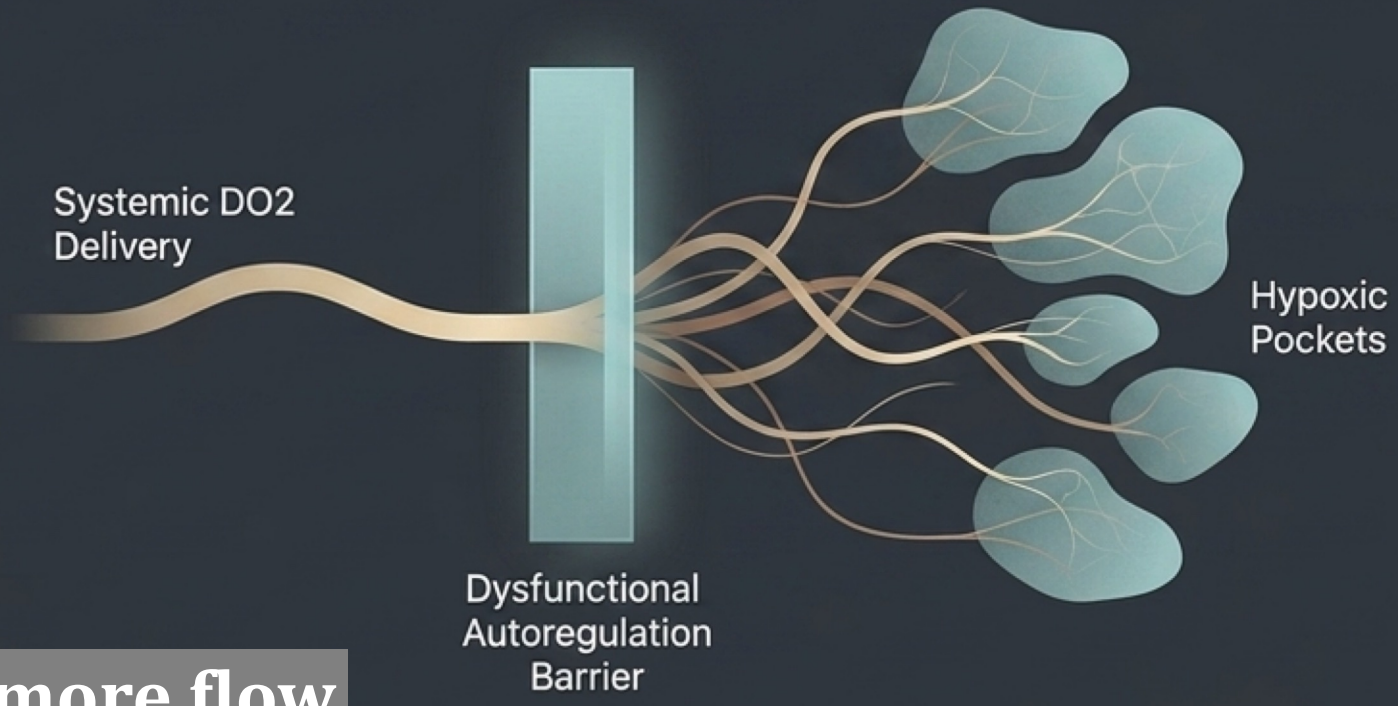
The 1979 Paradigm

Shoemaker proposed supranormal goals. Effective in hemorrhagic shock, but detrimental in sepsis.

DO2: 600 mL/min/m² | VO2: 170 mL/min/m² | CI: >4.5 L/min/m²

The Pathological Paradox

Sepsis introduces pathological flow heterogeneity. Dysfunctional autoregulation leads to hypoxic pockets and mitochondrial failure, rendering systemic DO2 maximization ineffective.



**Macrocirculation restored,
tissue still hypoxic.
You cannot open a shunt with more flow.**

Chasing Pressure Has Its Own Cost

THE VICIOUS CYCLE

More fluid → congestion → lower perfusion gradient

MAP 沒到 → 再給水
↓
鬱血 → 器官水腫
↓
把靜脈端墊高 = 自己降低灌流梯度
↓
MAP 還是沒到 → 又再給水

THE EVIDENCE FOR “LESS IS FINE”

Restrictive strategies cost nothing

CLASSIC 2022 · CLOVERS 2023
→ restrictive vs liberal：死亡率無差異

ANDROMEDA-SHOCK 2019
→ 8h 少 408 mL，器官功能更好

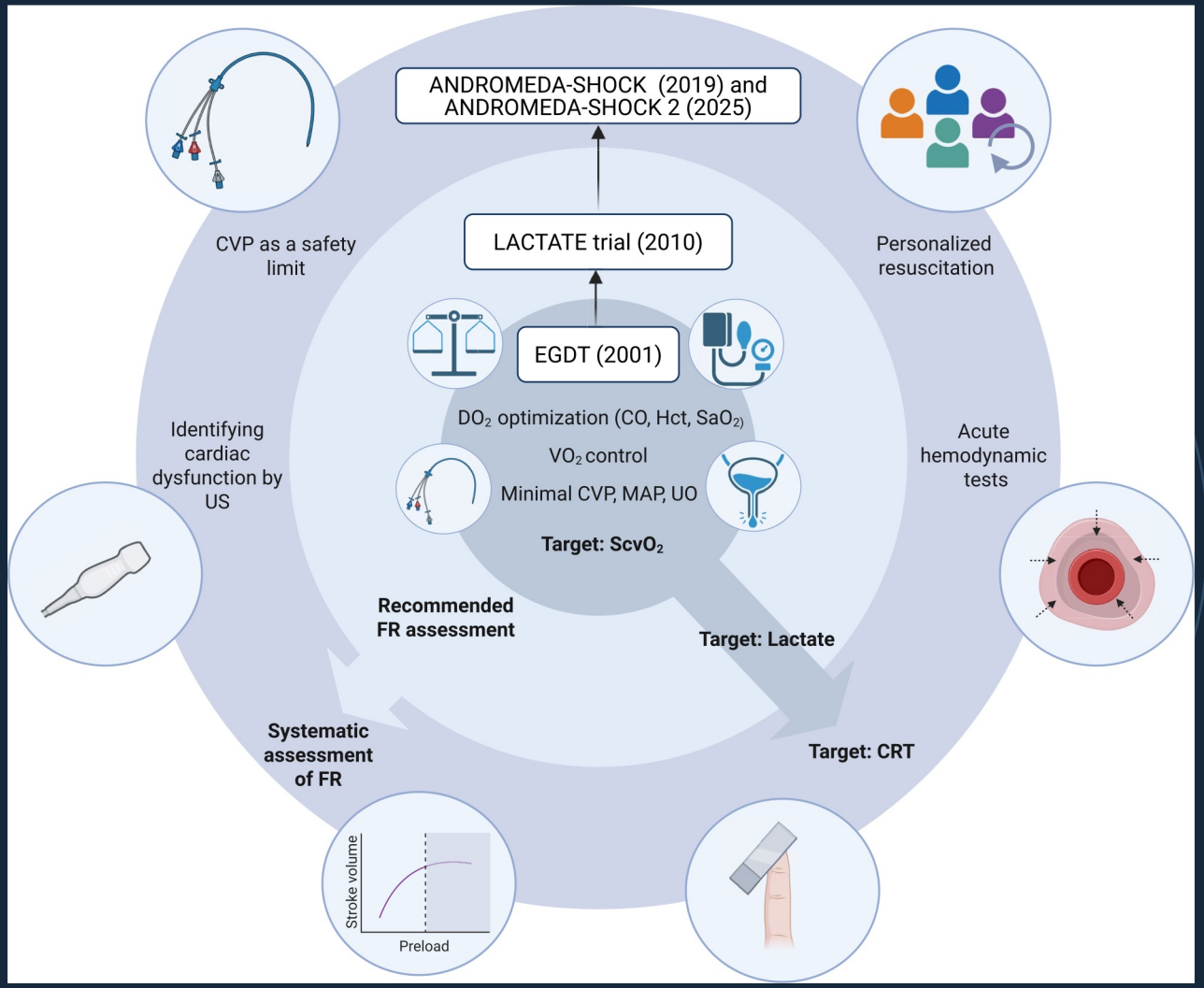
ANDROMEDA-SHOCK-2 2025
→ 6h 少 251 mL，CVP 較低

所以我們需要會說「stop」的 target。

CLASSIC 2022 · CLOVERS 2023 · ANDROMEDA-SHOCK 2019/2025.

II

The Candidate Targets



Beyond MAP: verify perfusion, phenotype and tolerance

A Layered Toolbox — Not "All Sensors at Once"

Basic 有沒有低灌流？

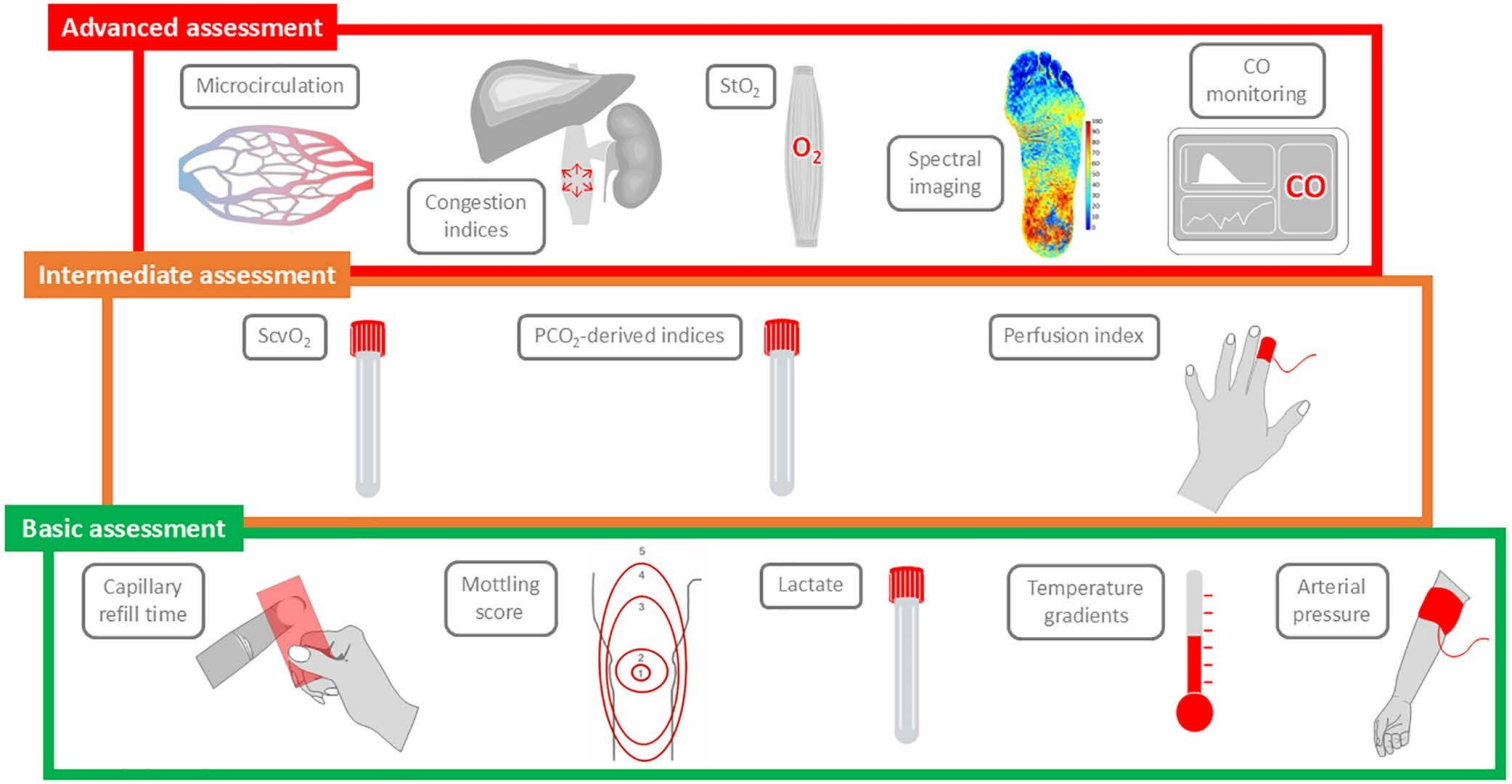
MAP · CRT · Mottling · Lactate · 溫度梯度

Intermediate 是流量問題，還是萃取問題？

$ScvO_2$ · Pv-aCO_2（ΔPCO_2）· Perfusion index

Advanced 機轉卡在哪一段？

CO monitoring · StO_2 · VExUS · 微循環影像 · Pcrit



Escalate on incoherence, not on a number

升級監測的時機不是「一開始就全上」，而是「生理不一致、且不確定性未解決」時，才往上一階。

Sanchez-Escalante C, Monnet X. Multimodal Perfusion Assessment. Crit Care Med 2026;54:1–8

ANDROMEDA-SHOCK — CRT vs. Lactate as the Target

STUDY POPULATION n = 424 · 28 ICUs / 5 countries · SEPSIS-3 早期敗血性休克 · 8 小時介入期 · CRT 每 30 分鐘、lactate 每 2 小時評估 · 兩組共用同一階梯式流程

Outcome	CRT	Lactate	Effect
28-day mortality	34.9%	43.4%	HR 0.75 (.55–1.02) p = .06
SOFA at 72 h	5.6	6.6	−1.00, p = .045
Fluids in 8 h	2359	2767	−408 mL, p = .01
Vasopressor test	28.8%	40.1%	−11.3%, p = .02

This is a negative trial. CRT targeted group → lower SOFA at 72h
Lactate targeted group → more fluids in 8h and vasopressor test
The endpoint decided the treatment intensity.

Hernández G, et al. ANDROMEDA-SHOCK. JAMA 2019;321:654–664 · Zampieri FG, et al. Am J Respir Crit Care Med 2020;201:423–429.

PART II · CRT

Why Capillary Refill Time Can Be the Anchor

THE STANDARDISED TECHNIQUE — **Glass slide + stopwatch**

玻片壓迫遠端指腹至皮膚變白並維持 10 秒，釋放後以碼錶計時回復原色所需時間 · > 3 秒為異常

Fast enough to steer

Minutes, not hours

CRT 每 30 分鐘可重測
Lactate 每 2 小時

復甦是動態過程， 需要動態訊號

Free and standardisable

10-sec compression,
> 3 sec abnormal

資源有限的環境也能做
兩個 ANDROMEDA 試驗同一標準

Linked to the microcirculation

與舌下微循環血流相關
與靜脈氧合指標相關
巨循環達標CRT仍可異常

A normal CRT tells you to stop — but only if everyone measures it the same way.
限制：低體溫、深膚色、周邊血管疾病、Raynaud、光線與操作者技巧。
目測不可靠：導入必須配套訓練與稽核（ANDROMEDA-SHOCK-2 因此排除 22 位）。

Hernández G, et al. JAMA 2019;321:654–664 · ANDROMEDA-SHOCK-2 Investigators. JAMA 2025;334:1988–1999 · Surviving Sepsis Campaign 2026

PART II · LACTATE

Lactate — A Great Prognostic Marker, a Poor Target

A safe substitute for $ScvO_2$

Jones 2010 · n = 300

Clearance ≥10% vs $ScvO_2$ ≥70%
院内死亡 17 vs 23%
差異 6%（−3 to 15）
未跨越 −10% 非劣性界值
抽血即可，免連續導管

Slow — and it drives treatment

ANDROMEDA-SHOCK 2019

8 小時多給 408 mL
Vasopressor test 40 vs 29%
72 小時 SOFA 6.6 vs 5.6
訊號恢復慢，復甦停不下來

Harmful once CRT is normal

Kattan 2020 · n = 184

T2 已 CRT 正常的次族群
28 天死亡 40 vs 23%
校正後 OR 3.3（1.5–7.1）
輸液 1000 vs 500 mL
Inodilator 16 vs 3%

前 6–12 小時流量依賴、讀得準；之後受廓清與代謝阻斷影響，CRT 正常後仍可高數小時。它回答「這個病人有多重」，不回答「現在還缺不缺灌流」。

Jones AE, et al. JAMA 2010;303:739–746 · Kattan E, et al. Ann Intensive Care 2020;10:114; Castro R, et al. J Crit Care 2026;91:155286.

PART II · $ScvO_2$

$ScvO_2$ — From Target to Modifier

WHY IT WAS DEMOTED

ProCESS · ARISE · ProMISe

三大 RCT 未能複製 EGDT 的存活益處；現代病人入 ICU 時多半已正常。

ITS ROLE NOW

A triage variable, not a target

分類與調整指標 ：
用來分辨這是流量問題，還是萃取問題

Low $ScvO_2$
Inadequate DO_2 — flow, Hb or SaO_2

Normal $ScvO_2$
The only “safe” zone —
still needs corroboration

High $ScvO_2$
Extraction failure —
shunt / mitochondrial dysfunction

ProCESS / ARISE / ProMISe · Jones AE, JAMA 2010.

PART II · $PV\text{-}ACO_2$

ΔPCO_2 — Flow Adequacy, Not Cardiac Output

PHYSIOLOGY

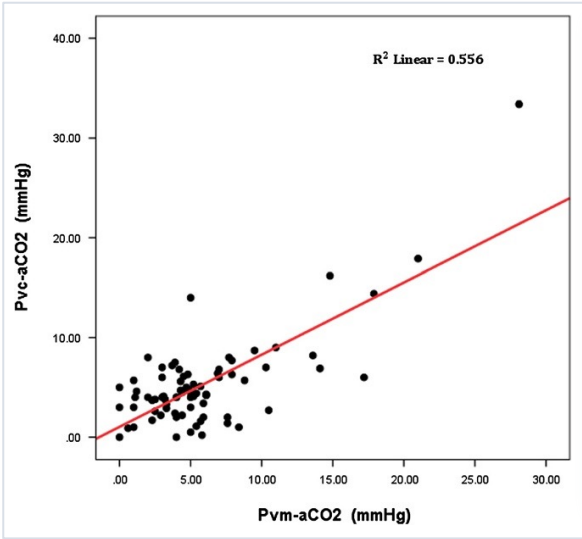
CO_2 elimination = $CO \times (CvCO_2 - CaCO_2)$

血流不足以清除產生的 CO_2 時上升，閾值 **6 mmHg**。隨血流動力學立即改變。

GOING FURTHER

$Cv\text{-}aCO_2$ / $Ca\text{-}vO_2$ ratio

CO 在推導中被抵消，**> 1.0 暗示厭氧代謝**：比單獨 ΔPCO_2 更能區分厭氧。



CAVEAT 1

Central ≠ mixed

r = 0.71 但 R^2 僅 0.556。臨床用的多是代理指標。

CAVEAT 2

Haldane effect

充氧血紅素對 CO_2 的親和力較低，血流增加時可能出現矛盾性上升。

CAVEAT 3

False negatives

Hyperdynamic status, 血流足以沖走 CO_2 時可正常，但組織仍可能缺氧。

Ospina-Tascón GA, et al. Crit Care 2013;17:R294

PART II · WHY IT WORKS

ΔPCO_2 Tracks Flow, Not Oxygenation

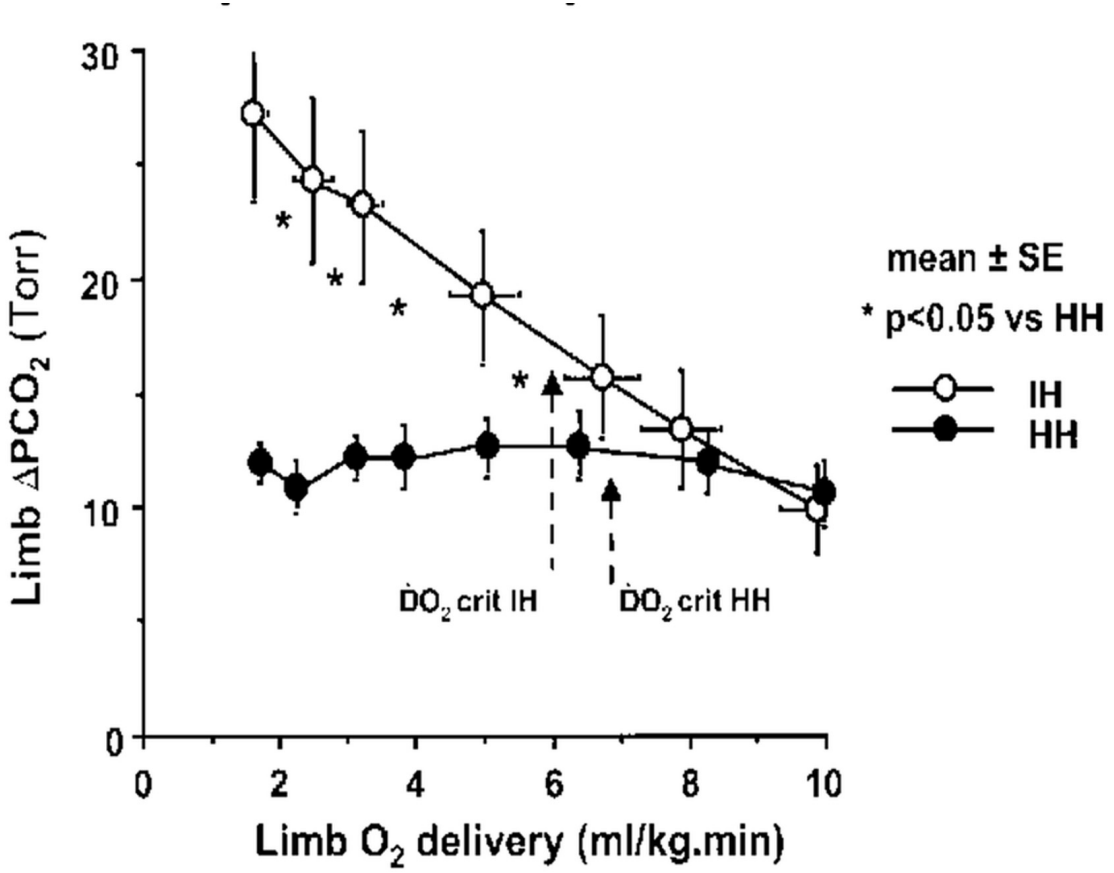


Fig. 6. Hindlimb ΔP_{CO_2} (outflow P_{CO_2} − inflow P_{CO_2}) as a function of

犬後肢模型：ΔPCO_2 對 DO_2，缺血性缺氧 vs 缺氧性缺氧

THE EXPERIMENT

Two ways to starve a limb of O_2

缺血性缺氧（IH）壓低血流量，
缺氧性缺氧（HH）壓低含氧量。
兩組的 DO_2 下降幅度與**ΔPCO_2**的關係

ONLY ONE RAISES THE GAP

IH 一路上升，HH 幾乎平坦

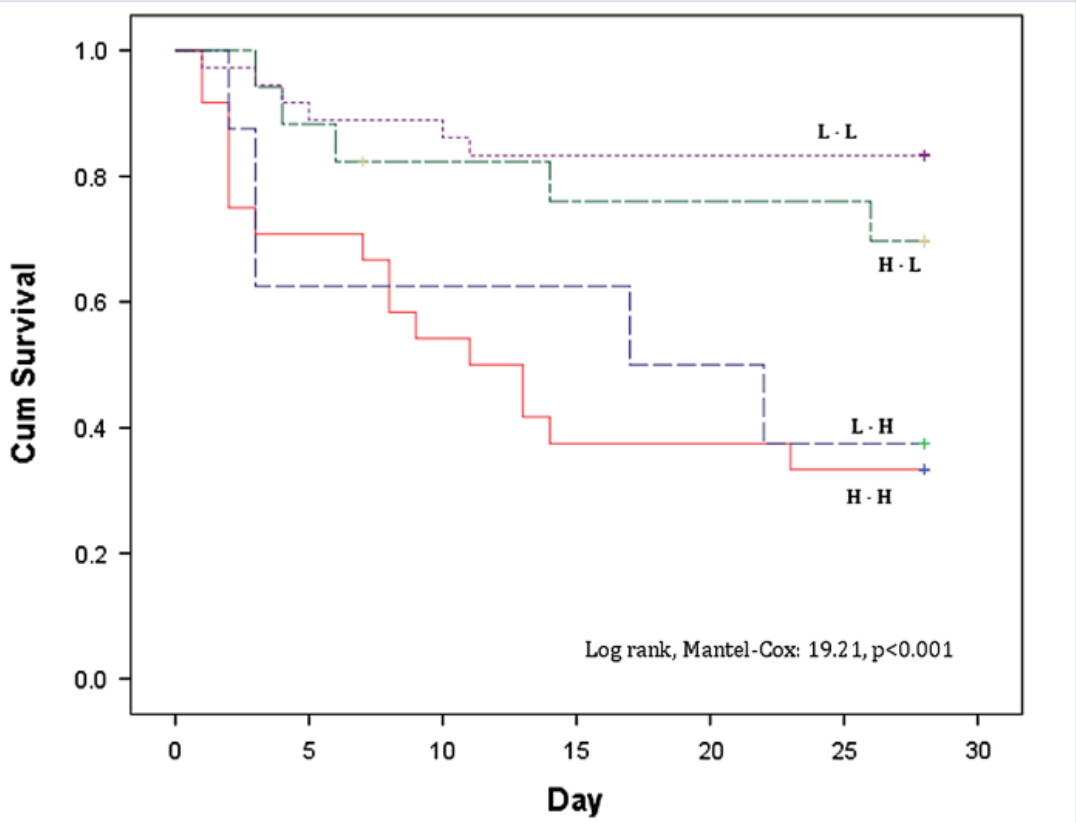
降血流時 ΔPCO_2 隨 DO_2 一路爬升；
單純降含氧量時，ΔPCO_2 幾乎不動。
兩組只有在 DO_2 crit 以下才交會。

WHAT IT MEANS AT THE BEDSIDE

Gap 高 = CO_2 沖不走 = 血流相對於代謝需求不足。它不告訴你氧合好不好，也不告訴你心輸出量是多少。

PART II · PV-ACO₂ OUTCOME

Persistently High ΔPCO₂ Predicts Death



STUDY POPULATION

n = 85 · single-centre prospective · all with pulmonary artery catheter · APACHE II ≈ 24 · 28-day mortality 37.6% · resuscitated to $ScvO_2$/SvO_2 and MAP targets

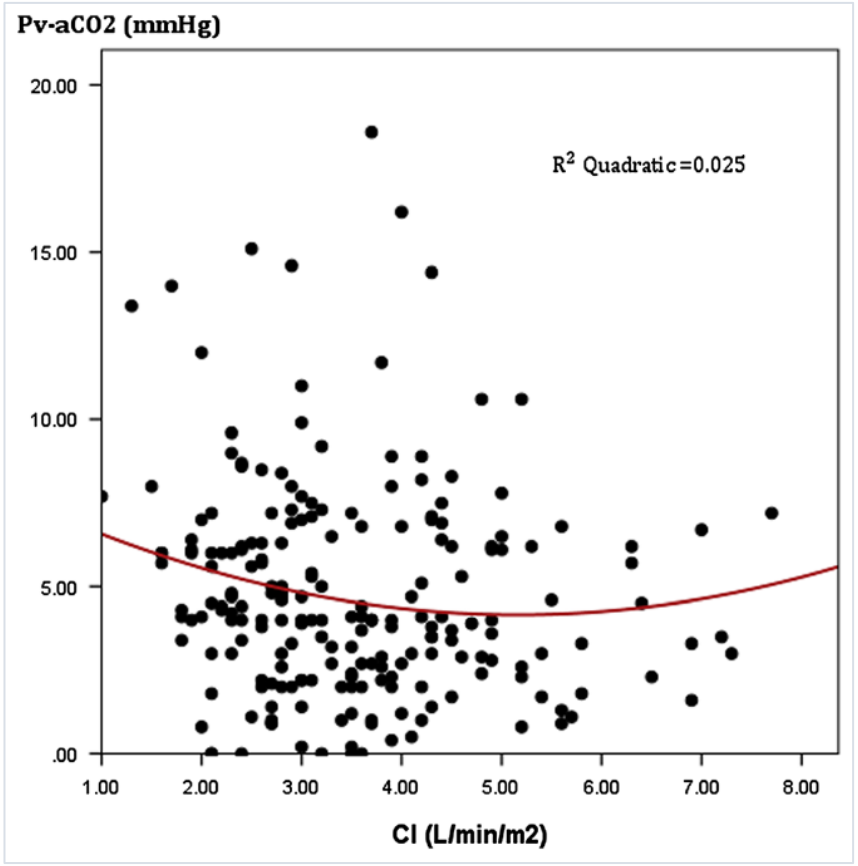
Day-28 mortality risk in patients who reached $ScvO_2$ ≥ 70% but kept ΔPCO_2 ≥ 6 mmHg

Time	Relative risk	95% CI	p
T0	1.77	0.97 – 3.22	.06
T6	**2.23**	1.20 – 4.13	.01
T12	**2.41**	1.42 – 4.10	.001

Higher day-3 SOFA ($p < .001$) and worse day-28 survival (log-rank 19.21, $P < 0.001$)
達標的 $ScvO_2$ 掩蓋了一群死亡風險兩倍以上的病人。

Ospina-Tascón GA, et al. Crit Care 2013;17:R294

ΔPCO_2 Is Not a Mirror of Cardiac Output



$R^2 = 0.025$

Agreement between cardiac index and ΔPCO_2 (Pearson r = 0.16, p < .01)

WHAT THIS MEANS

Normal CO does not exclude a high gap

這群病人 CO 在 24 小時內維持正常甚至偏高，ΔPCO_2 仍高。

THE MECHANISM

It measures distribution, not pump output

在 sepsis，ΔPCO_2 反映的是「血流分佈夠不夠沖走 CO_2」。

動物與人體資料顯示，。
決定組織 CO_2 累積的主要因素是微循環血流，而非心輸出量

所以應該是「相對血流不足」，不是「心輸出量不夠」。

Ospina-Tascón GA, et al. Crit Care 2013;17:R294.

$ScvO_2$ × ΔPCO_2 — The Four Quadrants

	$\Delta PCO_2 \leq 6$ mmHg	$\Delta PCO_2 > 6$ mmHg
$ScvO_2$ < 70%	**High demand / Low O_2 content** 血流尚可但含氧量太低供需失衡 → 查 Hb、SaO_2，降低 VO_2。	**Inadequate DO_2 — classic low flow** **Stagnant dysoxia**, 最單純的一格 → responsive 就給水，否則考慮強心
$ScvO_2$ ≥ 70%	**Extraction / mitochondrial failure** **Cytopathic hypoxia**, 流量夠了組織用不了 → 停止 flow 加碼，避免 fluid overload。	**Flow heterogeneity — danger zone** RR 2.23–2.41。$ScvO_2$ 正常是假象，微循環分流嚴重，局部血流停滯 → 查 VExUS，進一步優化 Perfusion。

$ScvO_2$ asks if enough O_2 arrived. ΔPCO_2 asks if it was distributed.

PART II · A SAFETY GATE

Fluid Responsiveness Is Not a Target

PLR — THE REVERSIBLE TEST

Passive leg raise ≈ 300 mL autotransfusion

CI 或 SV 上升 > 10–12% 為陽性。可逆、可重複、不受通氣模式限制。

PPV / SVV

Limitation

需控制型通氣、Vt ≥ 8 mL/kg、竇性心律、無自主呼吸、無右心衰竭。

THE PRINCIPLE

Responsive does not mean it needs fluid.

約 50% 的健康人也是 fluid responsive。

每一次給水之前都先評估 fluid responsiveness 。

它回答「給了會不會有反應」，

該不該給，由灌流指標決定。

PART II · THE FLUID DECISION

Give Fluid Only When Three Conditions Align

三個條件同時成立才給——任何一個不成立，給水就是在製造下一個問題。

HYPOPERFUSED

① 有問題要治

CRT 延長、mottling、少尿、意識改變或器官功能惡化。數字異常不等於灌流不足。

RESPONSIVE

② 流量真的能增加

PLR 或輸液試驗使 SV / VTI 上升約 10% 以上。血壓上升不算數。

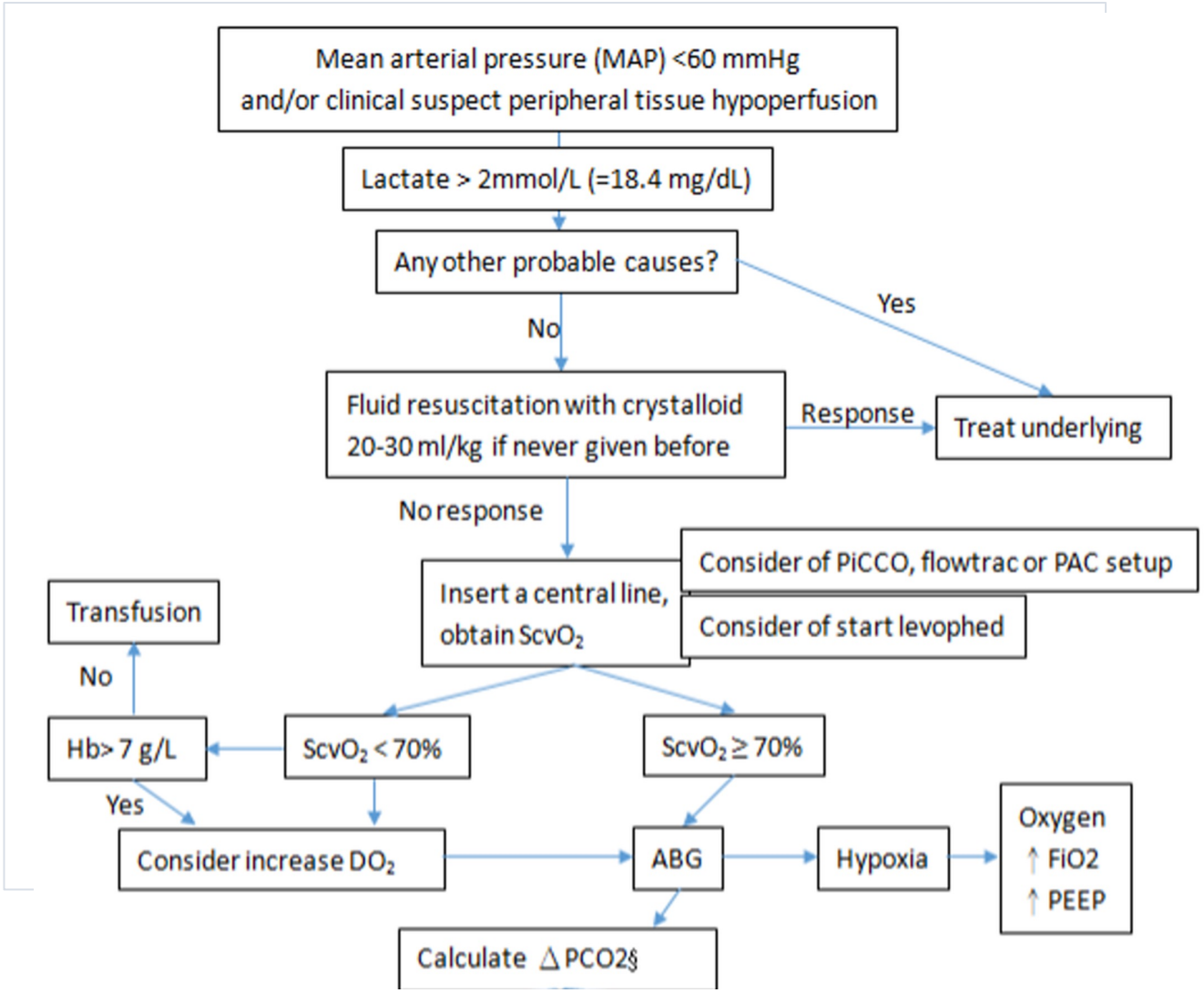
TOLERANT

③ 鬱血風險可接受

VExUS、肺部超音波、右心功能。有反應不等於需要給。能承受才是最後一關。

All three → a small, reassessed fluid challenge. Any one missing → do something else.
只滿足前兩項就給水，是過度復甦最常見的入口。

SHOCKWAY at MMH — The Resuscitation Backbone



THE TRIGGER

MAP < 60，或懷疑灌流不足

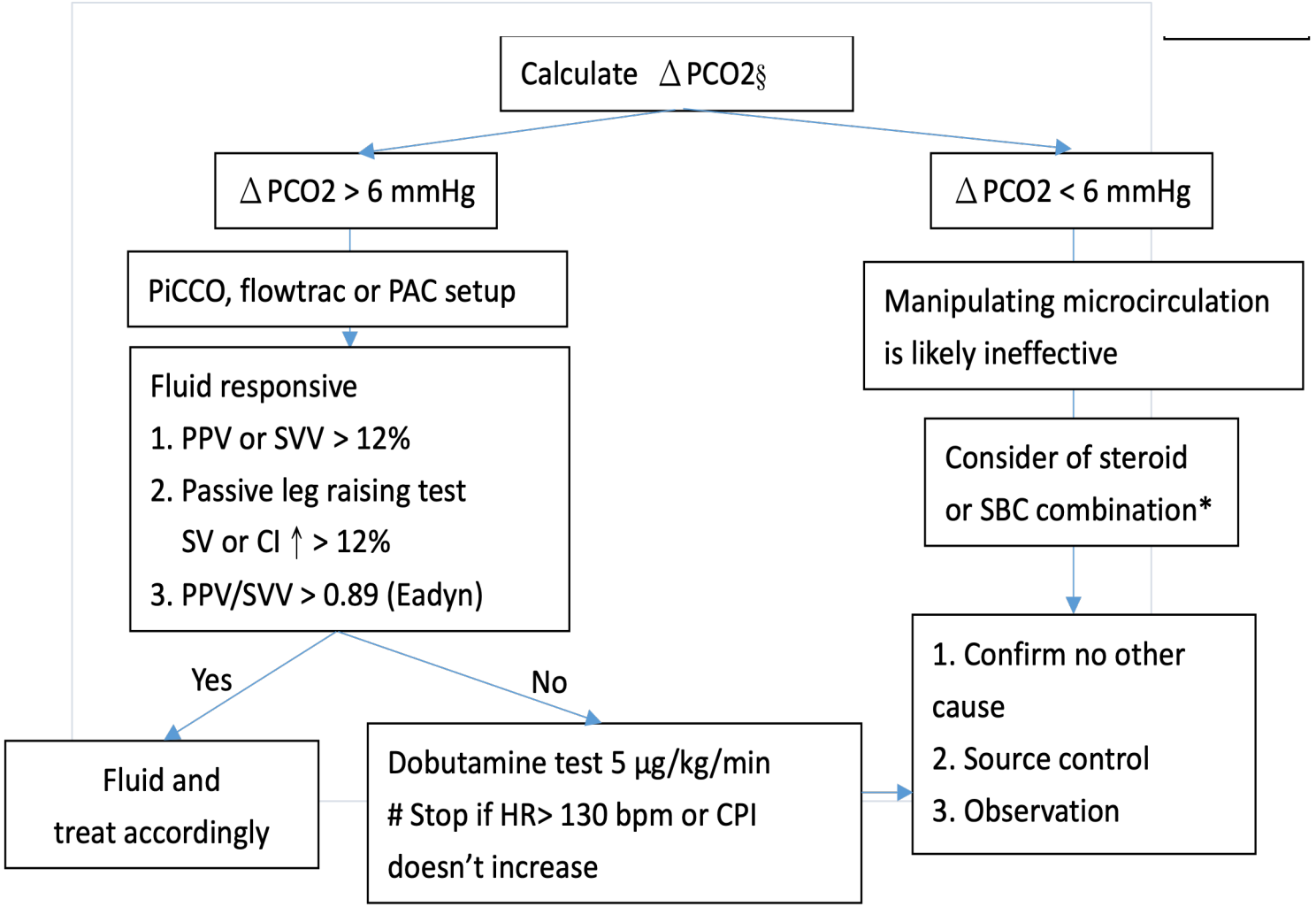
再加上 lactate > 2、排除其他可能原因，然後晶體液 20–30 mL/kg。這一段跟大多數單位一樣，是 EGDT 留下的骨架。

THE FIRST FORK

$ScvO_2$ 70%

低於 70% 走 Hb 7 判斷輸血與提升 DO_2；達到 70% 就直接進 ABG。這是 2001 年Rivers 留下的第一個岔路

Where ΔPCO_2 Takes Over



THE TWO ARMS

$\Delta PCO_2 > 6$ 找血流

高 gap 走 fluid responsiveness 與dobutamine test

$\Delta PCO_2 < 6$ 換方向

低 gap 視為操作微循環無效，轉向類固醇與感染源控制。

Evolution of Septic Shock Resuscitation Concepts:
From Single Targets to Personalized Physiology-Guided Therapy

	2001	2010	2014	2019	2022	2025
Key trials Milestones	**EGDT** $ScvO_2$-guided resuscitation	**LACTATE** Lactate-guided resuscitation	**SEPSISPAM** MAP Targets	**ANDROMEDA-SHOCK** CRT targeted resuscitation	**CLASSIC** Restrictive vs. liberal fluid strategies	**ANDROMEDA-SHOCK 2** CRT targeted personalized resuscitation
Physiological paradigm	**Optimizing global oxygen delivery** Correcting low $ScvO_2$ by improving DO_2 to restore DO_2/VO_2 balance	**Metabolic resuscitation** Hyperlactatemia as a marker of tissue hypoperfusion and resuscitation target	**Higher pressure targets** Higher perfusion pressures might improve tissue perfusion	**CRT as a reperfusion signal** CRT normalization may be a signal of successful reperfusion	**Avoiding fluid excess** Restrictive fluids might prevent fluid-induced harm	**Toward tailored, physiology-guided care** Sequential, multilayered assessment targeting on pathophysiology-guided interventions
Conceptual evolution	**Perfusion-oriented resuscitation** Use of physiological information to guide resuscitation	**From marker to target** Shift from a prognostic marker to a quantifiable treatment target	**Context defines MAP meaning** Interpreting MAP requires a physiological perspective	**Targeting peripheral perfusion** CRT as a target to tailor fluids, vasopressors and inotropes	**Fluid therapy needs individualization** Fluid therapy to become a physiology-guided, individualized intervention	**Personalization of resuscitation** Personalized, phenotype-driven resuscitation with serial reassessment
Enabling tools	$ScvO_2$ measurement	Lactate measurement		Capillary refill time	Fluid responsiveness	Critical care echocardiography

Hernandez *et al. Critical Care* (2026) 30:400

III

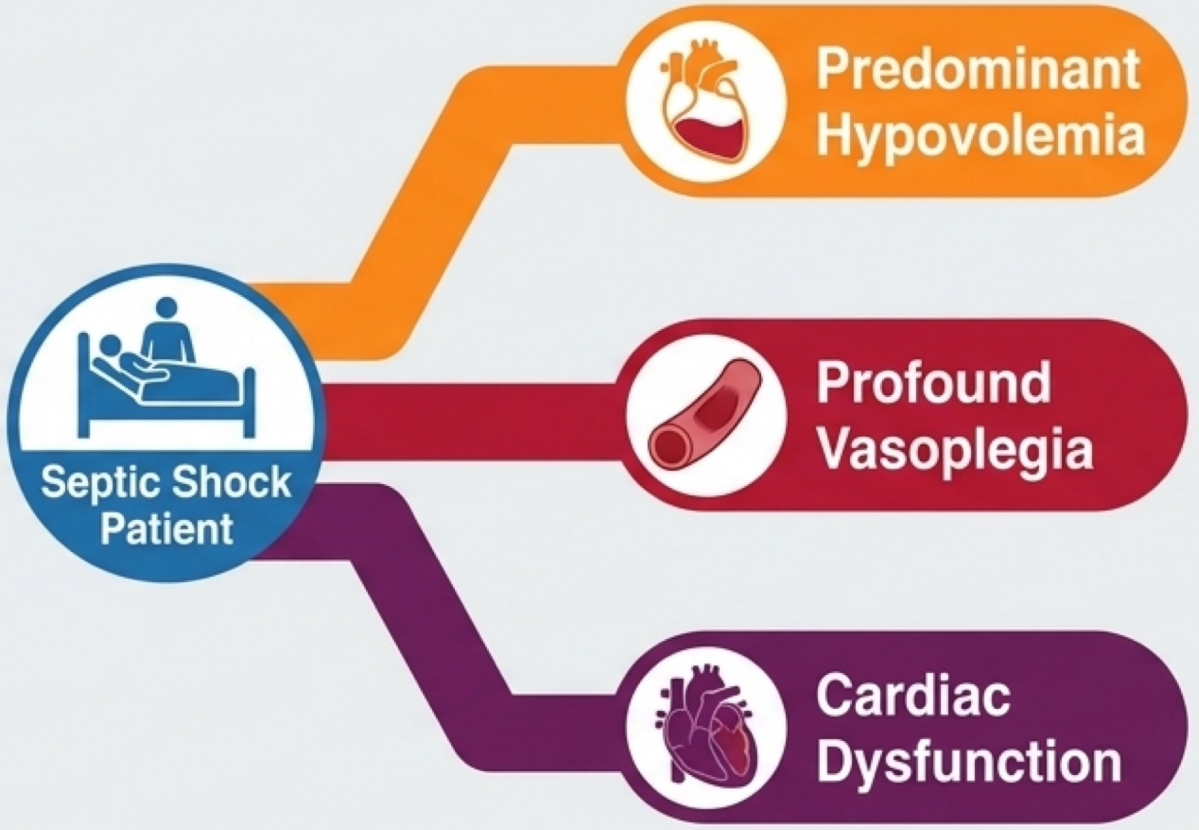
CRT-PHR: The Trial, Then the Protocol

個人化血流動力復甦

The Failure of Universal Thresholds

⚠ The Limitation

Recent trials examining non-personalized strategies (universal liberal vs. restrictive fluids [CLASSIC], universal MAP targets [SEPSISPAM]) have failed to consistently improve patient-centered outcomes.



Key Insight: *Identical Mean Arterial Pressures (MAP) can represent entirely different microcirculatory flow states depending on the patient's individual critical closing pressure (P_{crit}) and vascular tone.*

ANDROMEDA-SHOCK-2 — How the Trial Was Built

STUDY POPULATION n = 1467 · 86 ICUs / 19 countries ·
符合條件後 4 小時內收案 · CRT-PHR 720 vs usual care 747 · 6 小時介入期 · 2022–2025

Usual care, not lactate

The comparator changed

AS-1 比 lactate，AS-2 比usual care
對照組 62% 做過 fluid responsiveness
68% 做過基本心臟超音波
這不是一個被放生的對照組

Hierarchical outcomes, win ratio

Death → organ support → LOS

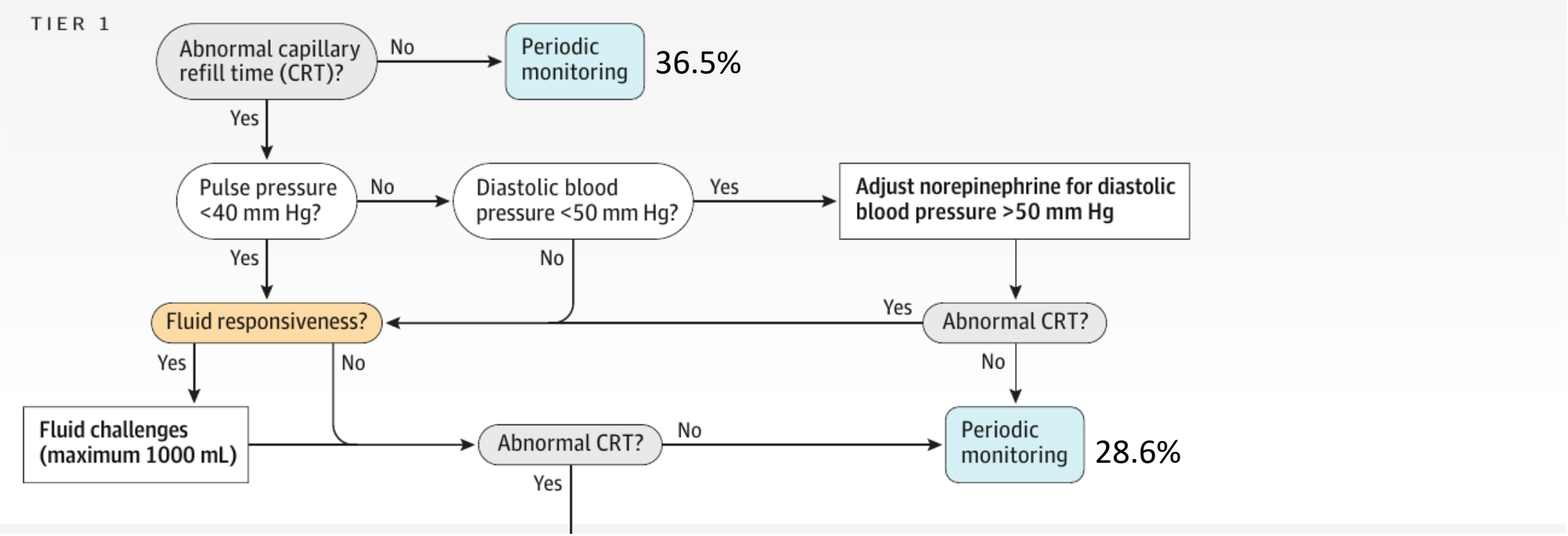
以 APACHE II 中位數分層
每一對病人依序比較這三層
先比死亡；兩人都死 = early tie
都存活才比器官支持天數
最後才比住院天數

A win ratio counts pairs— it is not a hazard ratio.
所以它回答的是「贏的配對多多少」，不是「死亡率降多少」。

ANDROMEDA-SHOCK-2 Investigators. JAMA 2025;334:1988–1999

PART III · THE PUBLISHED ALGORITHM

CRT-PHR Tier 1 — Tone and Stroke Volume



STEP 1

Pulse pressure < 40 ?

是 → 測 fluid responsiveness，陽性才給水（上限 1000 mL）

STEP 2

DAP < 50 mmHg ?

是 → NE 上調至 DAP > 50，不是拉到 MAP 80。

EXIT

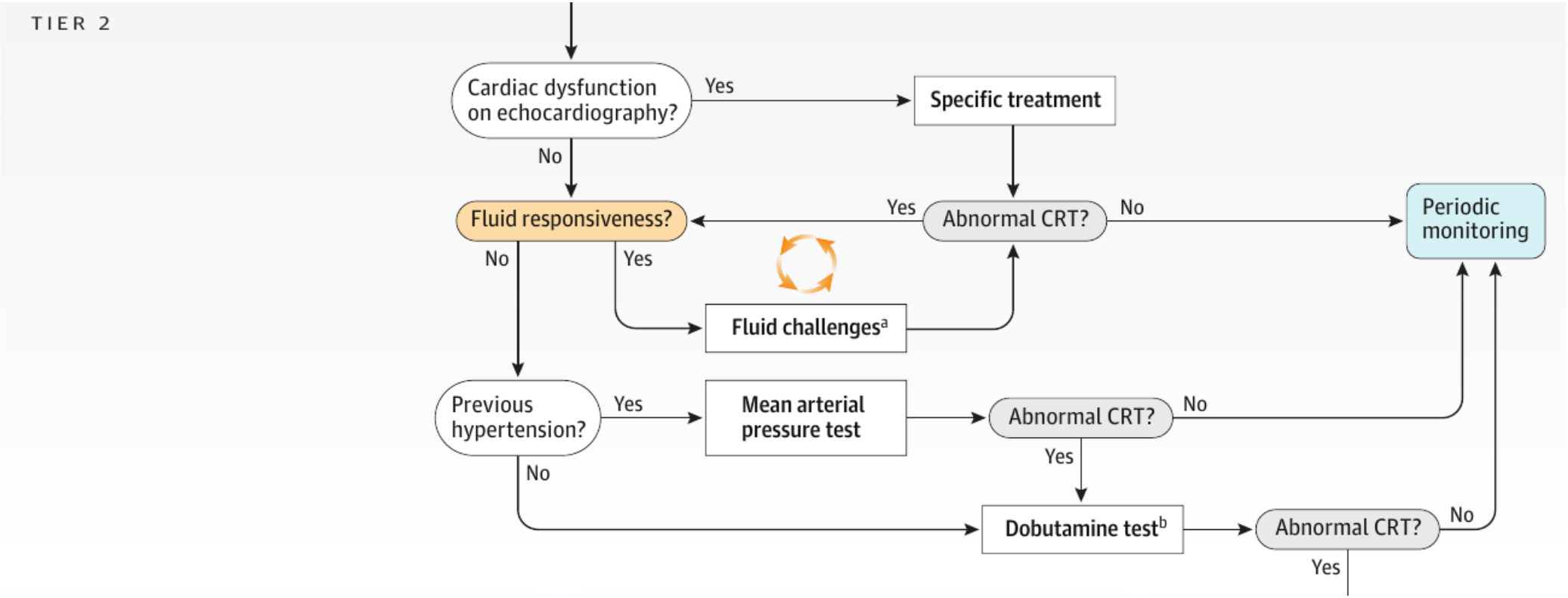
CRT normal → monitoring

65% 的病人在Tier 1 就結束

ANDROMEDA-SHOCK-2 Investigators. JAMA 2025;334:1988–1999

PART III · THE PUBLISHED ALGORITHM

CRT-PHR Tier 2 — Pump and Reversible Tests



STEP 3

Basic echocardiography

有左心 / 右心功能障礙 → 針對性治療。

STEP 4 · REVERSIBLE

MAP test | Dobutamine test

各 1 小時，以 CRT 判讀，沒反應就撤。

Only 35% of patients enterTier 2

仍失敗才進 rescue therapies

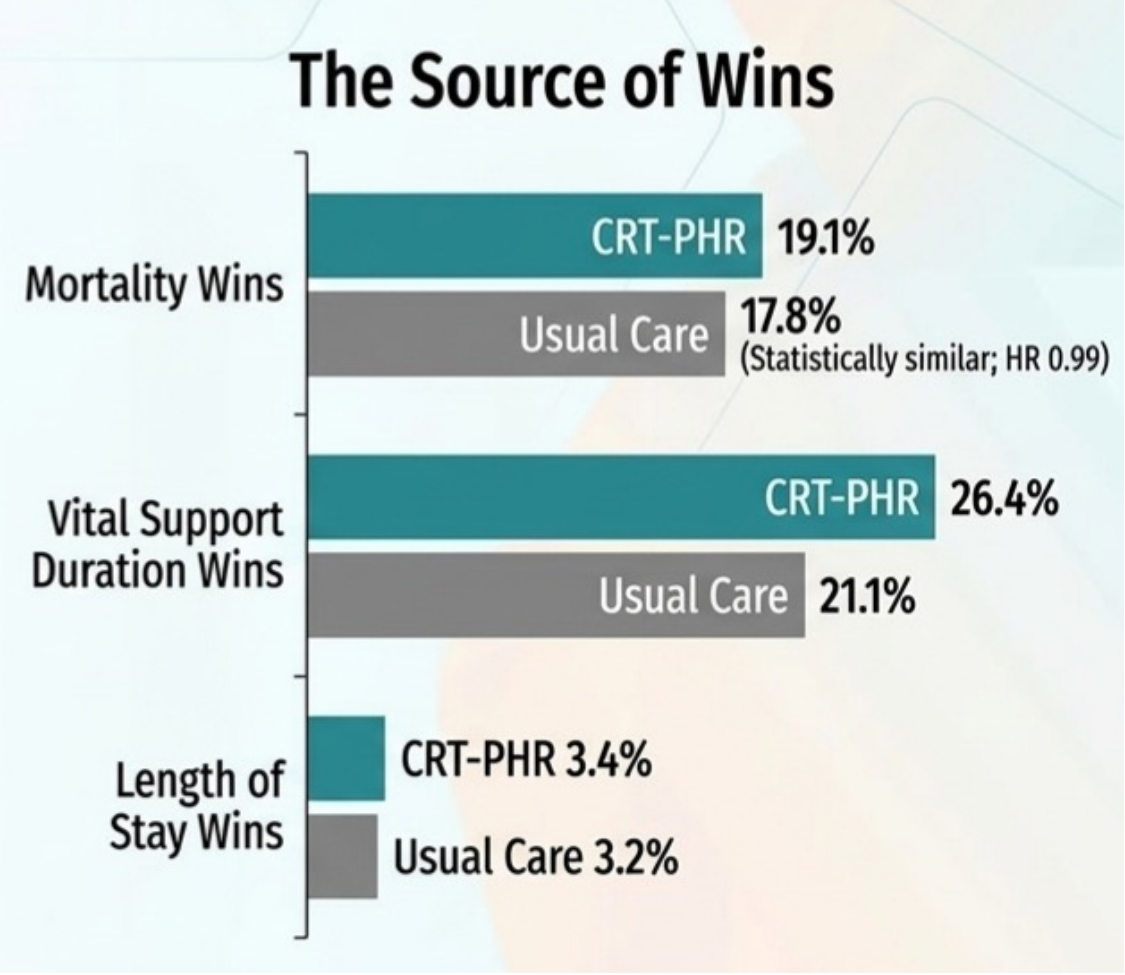
ANDROMEDA-SHOCK-2 Investigators. JAMA 2025;334:1988–1999

PART III · THE PROOF

ANDROMEDA-SHOCK-2 — The Primary Outcome

STUDY POPULATION

n = 1467 · 86 ICUs / 19 countries ·
符合條件後 4 小時內收案 · CRT-PHR 720 vs usual care 747 · 6 小時介入期 · 2022–2025



Win ratio 1.16

95% CI 1.02 – 1.33 p = .04

WHERE THE WIN CAME FROM

Organ support duration, not survival

死亡 19.1 vs 17.8%
器官支持天數 26.4 vs 21.1%

Secondary outcome

No survival benefit

28D all cause mortality 26.5% vs 26.6% (HR= 0.99)

ANDROMEDA-SHOCK-2 Investigators. JAMA 2025;334:1988–1999, Figure 3.

PART III · THE MECHANISM

What Actually Changed at the Bedside

Variable at 6 h	CRT-PHR	Usual care	Δ
CRT normalisation	85.9%	61.7%	**+24.2**
Resuscitation fluid	595 mL	847 mL	**−251**
Dobutamine use	12.3%	5.3%	+7.0
Central venous pressure	9.1	9.8	−0.6
Lactate	3.2	3.5	−0.3

The protocol effectively achieved its target.
The benefit comes from stopping earlier.

ANDROMEDA-SHOCK-2 · Table 2, protocol footprint at 6 hours.

INTERPRETATION

Less fluid, more targeting

更精準的分型換來更少的經驗性輸液及更針對性的強心劑。

FEASIBILITY

It survived contact with reality

Deviation 15%、violation 僅 6%。

PART III · ONE-PAGER

The Complete Algorithm

0 MAP ≥ 65 mmHg | antibiotics | source control

1 CRT ≤ 3 sec? | lactate and ΔPCO_2 corroborate — they are not gates

2 ① PP < 40 → fluid responsiveness | DAP < 50 → norepi to DAP > 50
② $ScvO_2 \times \Delta PCO_2$ ③ POCUS

3 MAP test 80–85 (chronic HTN, 1 h) | Dobutamine 5 µg/kg/min (1 h)

4 VExUS | congestion | active fluid removal

Move down a step only when physiology is incoherent.

STEP 0–1 · FLOOR & PERFUSION CHECK

A Normal CRT Is a STOP Signal

STEP 1 問的不是「lactate 降了沒」，而是「灌流恢復了沒有」
CRT 是首選工具，lactate 與 ΔPCO_2 是佐證。

	LACTATE 下降 / 正常	LACTATE 仍高
CRT ≤ 3 sec	**Stop — high confidence** 不再加水、不再加壓；每小時重新評估 開始考慮 de-resuscitation（Step 4）	**Stop escalating anyway** Kattan 2020：續追 lactate，死亡 40 vs 23% 非灌流原因：source control、Type B、肝腎廓清
CRT > 3 sec	**Verify before you act** 先確認量測：玻片、10 秒、碼錶 排除低體溫、周邊血管疾病、Raynaud、深膚色	**Escalate — high confidence** 兩個訊號同向，不需再猶豫 → Step 2：PP · DAP → 血氣 → echo

Stop escalating — not stop watching.
CRT 正常者 28 天死亡率仍有 30%（Kattan 2020）。
在 CRT 標準化之前，這一步只能用 lactate 趨勢與 ΔPCO_2 執行。

ANDROMEDA-SHOCK-2, JAMA 2025;334:1988–1999 · Kattan E, et al. Ann Intensive Care 2020;10:114

STEP 2 · PHENOTYPE

Three Layers, Cheapest First

Arterial line only

Layer 1 · PP and DAP

PP < 40 → stroke volume 偏低
先測 fluid responsiveness，
陽性才給 500 mL / 30 min

DAP < 50 → 血管張力不足
NE 上調至 DAP > 50，
不是拉到 MAP 80

One blood gas pair

Layer 2 · $ScvO_2$ × ΔPCO_2

$ScvO_2$ 問「氧夠不夠送到」
ΔPCO_2 問「送得均不均勻」

兩者皆正常 → 不是流量問題
夜班可得，不吃操作者技術

Echo, POCUS

Layer 3 · pump and filling

分辨左心 / 右心功能障礙
排除阻塞性病灶
單一 IVC 直徑不決定輸液
仍無異常 → 進 Step 3

最耗人力，留給前兩層
無法回答的病人

CRT tells you whether to do it at all.
每一層做完都先回頭問 CRT 有沒有正常化。

ANDROMEDA-SHOCK-2, JAMA 2025;334:1988–1999

STEP 3 · REVERSIBLE TEST

Try for One Hour — Withdraw If No Response

MAP test

AS-2 protocol · success ≈ 50%

僅限慢性高血壓者NE 暫時上調至
MAP 80–85，維持 1 小時
CRT 正常化 → 維持到療程結束
未改善 → 調回原劑量，進入下一步

Dobutamine test

Fixed low dose · success ≈ 50%

5 µg/kg/min，固定劑量不 titrate
維持 1 小時後重讀 CRT, ΔPCO_2
Pellikka 1995, 健康人 CO 平均上升 27%
只有反應者才留下來

OPTPRESS refuted a fixed high MAP held for 72 hours — not a one-hour reversible test.
這是生理試探，不是治療策略。

ANDROMEDA-SHOCK-2 Tier 2（JAMA 2025;334:1988–1999）· Endo A, et al. OPTPRESS. Intensive Care Med 2025;51:883–892

STEP 4 · STOP & REMOVE

The Step That Says Enough

The stopping rules

Any one is enough

① CRT 已正常化
② Fluid unresponsive
③ 靜脈鬱血會降低器官的灌流梯度

VExUS rules congestion in

Not out — sensitivity 27%

Grade 3 = IVC ≥ 2 cm plus severe Doppler abnormality in ≥ 2 veins, +LR 6.37, Specificity 96%
CVP ≥ 12 的 +LR 僅 1.91
源自心臟手術族群

Then start removing

SSC 2026 · new statement
急性期後主動移除液體

Every step above answers “what more”.
This one answers “enough”.

Beaubien-Souligny W, et al. Ultrasound J 2020;12:16 · ANDROMEDA-SHOCK-2, JAMA 2025

Back to the Patient

MAP 68 (on target)　$ScvO_2$ 74% (on target)　CRT 5 sec　$Pv\text{-}aCO_2$ 8.5 mmHg
Lactate 4.2　CVP 11

WHICH QUADRANT?

Bottom right — flow heterogeneity

$ScvO_2 \geq 70\%$ 且 $\Delta PCO_2 > 6$。

74% 的「正常」是假象：這正是 day-28 死亡 RR 2.23 的那一群人。

四象限就是 Step 2 的第二層。

✕ Blind fluid bolus

先驗 fluid responsiveness；CVP 11 已不低。

✕ Blind MAP escalation

除非慢性高血壓，且以 1 小時可逆 test 進行。

✓ Phenotype first (PP / DAP → gas → echo)

再決定給水、加壓，還是 inotrope。

✓ Read the response with CRT

不是用 lactate，也不是用 MAP。

✓ Check the venous side (VExUS)

這是 Step 4：確認鬱血沒有在拖後腿。

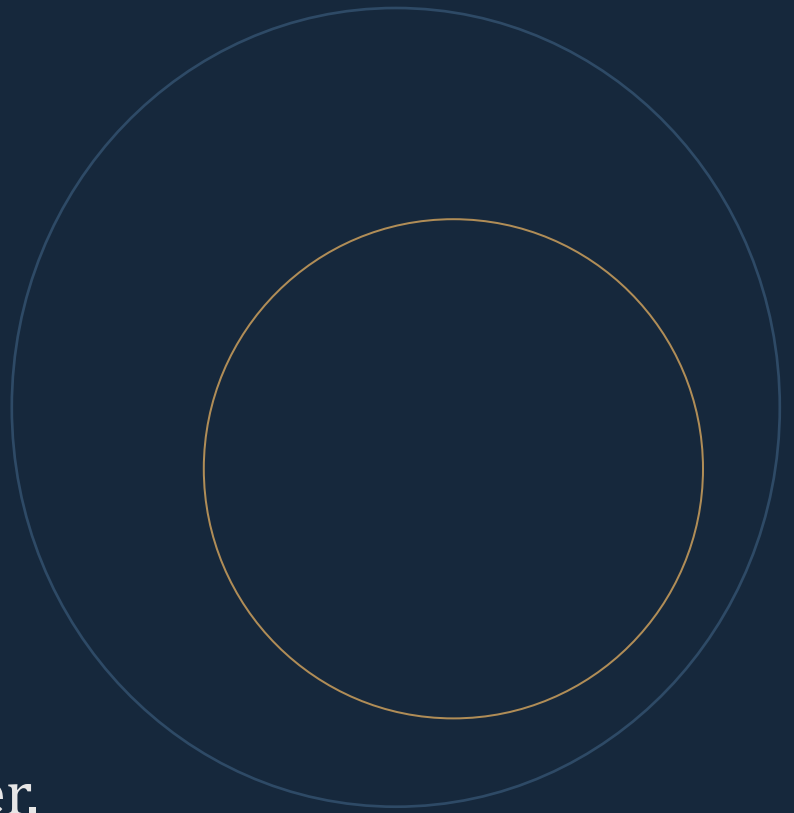
TAKE-HOME

65 or Not ?

1. **65 is not proven right — everything above it is proven wrong.**
2. **On-target pressure proves nothing about perfusion.**
3. **Escalate on incoherence, not on a number.**
4. **The endpoint you choose decides how hard you treat.**
5. **The gain of this decade is doing less.**

65 是安全下限，不是復甦終點。真正的 target 是「被驗證過的灌流反應」，用最低代價達成。

MAP opens the gates.
Flow carries the blood.
65 is where you start.
Perfusion is where you stop.



Not new drugs. Not new devices.
A deeper understanding of the tools we already had.
Target the patient's response — not the monitor's number.

Thank you · Questions & Discussion

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