

出國報告(出國類別:開會)

美國亞特蘭大心臟醫學會年會 2024
出國參加國際會議報告

服務機關：臺北榮民總醫院 麻醉部

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派赴國家：美國亞特蘭大

出國期間：113.4.6 ~ 113.4.9

報告日期：113.5.15

摘要：

本次出國參加國際會議的目的是為了發表與重症醫學部周睿信醫師及心臟內科黃柏勳主任共同研究的成果於美國心臟醫學會(American College of Cardiology)2024年會。因為心臟醫學也與麻醉醫學密切相關，也希望能利用這個機會吸收相關的新知與學術交流。會議為期 4/6-8，與周醫師一同前往。

職非常感謝院內、部內長官的支持，心臟內科前輩同事的指引，得以出國開會，一窺廟堂。從心臟醫學的新藥品新醫材的發展可以看到商業資本的投入，許多醫療機構集合研究資源和充足的病人族群才能獲得足夠的實證，因此美國心臟醫學年會此行的心得，使我們麻醉科醫師在開刀房中萬一遇到相似的情況可以做為參考以服務外科的病人。

關鍵字：美國、亞特蘭大、心臟醫學會、麻醉醫學

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本文

目的

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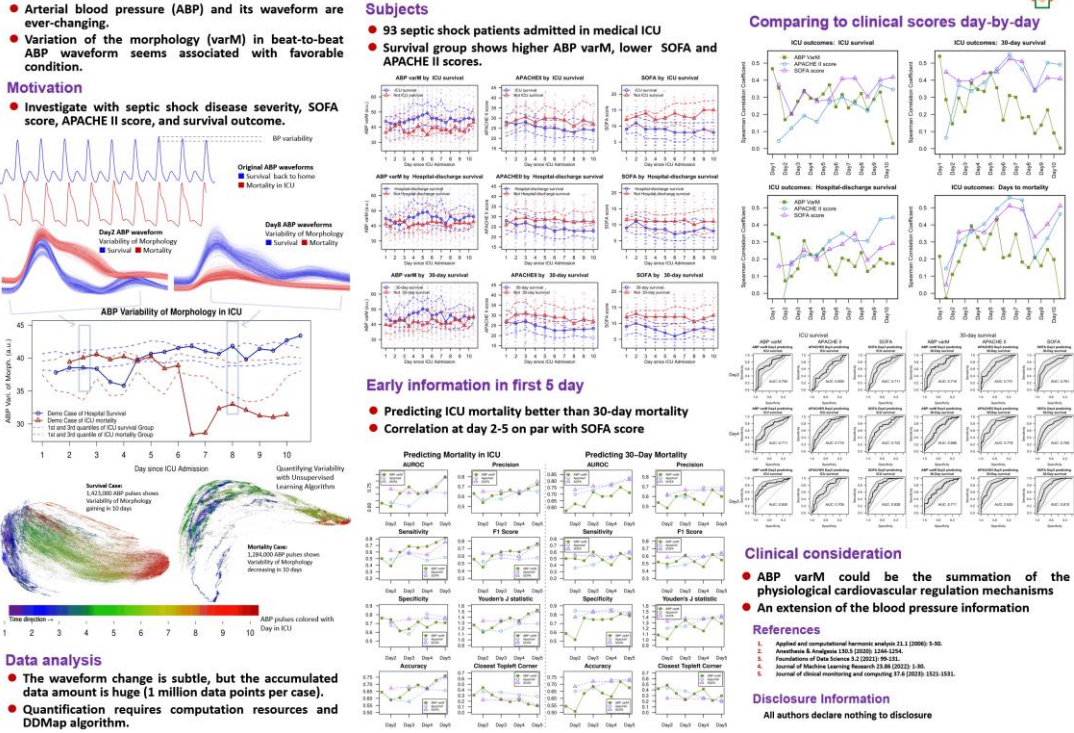
過程

本屆會議在美國亞特蘭大 Atlanta Convention Center 舉辦。心臟醫學相關議題多面，會議議程有多個 topics 平行進展，我們選擇 cardiology critical care medicine 相關的議程，也與臨床麻醉較有關連。

海報論文發表

本次發表的研究是建立動脈血壓波形訊號與加護病房敗血症癒後的關係，血壓波形是整個心血管系統的多狀態的整合和投影，每一個心跳就會產生一次血壓脈波^{1,2}。把每個脈波的變化和病人的狀況相關聯，我們發現變化的程度愈多樣複雜則臨床上的狀況也愈好。因為一次住院期間平均一位病人就有超過十萬個脈波產生，是大量的資料，所以在分析時也我們也得同時發展演算法以適切利用現今計算資源 (computation resource)的進展³。

Variability of morphology derived from arterial blood pressure waveform is associated with ICU and in-hospital mortality in septic patients
 Ruey-Hsing Chou^{1,2}, Yu-Ting Lin³, Shen-Chih Wang³, Cheng-Hsueh Wu^{1,2}, Po-Hsun Huang¹
 1. Division of Cardiology, 2. Department of Critical Care Medicine, 3. Department of Anesthesiology, Taipei Veterans General Hospital, Taipei, Taiwan



海報內容

因為主要的發現與臨床醫學有關而血壓波形與心臟醫學有關，所以選擇在美國心臟醫學會發表。以下將會議論文附上：

Conference abstract

Variability of morphology derived from arterial blood pressure waveform is associated with ICU and in-hospital mortality in septic patients

Yu-Ting Lin, Ruey-Hsing Chou, Shen-Chih Wang, Cheng-Hsueh Wu, Po-Hsun Huang, Hau-Tieng Wu

Background:

The ever-changing arterial blood pressure (ABP) offers vital assessment in intensive care unit (ICU). We investigated a new kind of waveform information in this study: variation of the morphology in beat-to-beat ABP waveform. We hypothesis the variability of ABP waveform morphology is associated with disease severity and survival outcome in septic patients.

Methods:

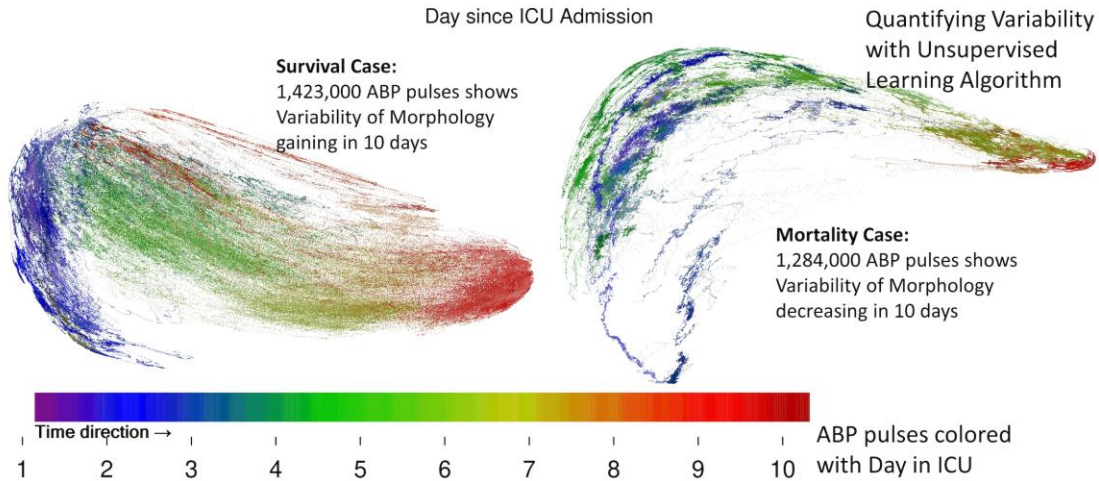
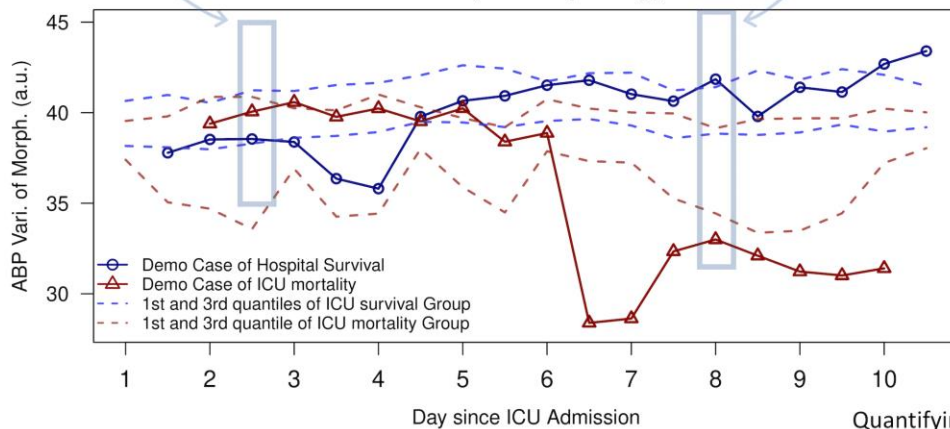
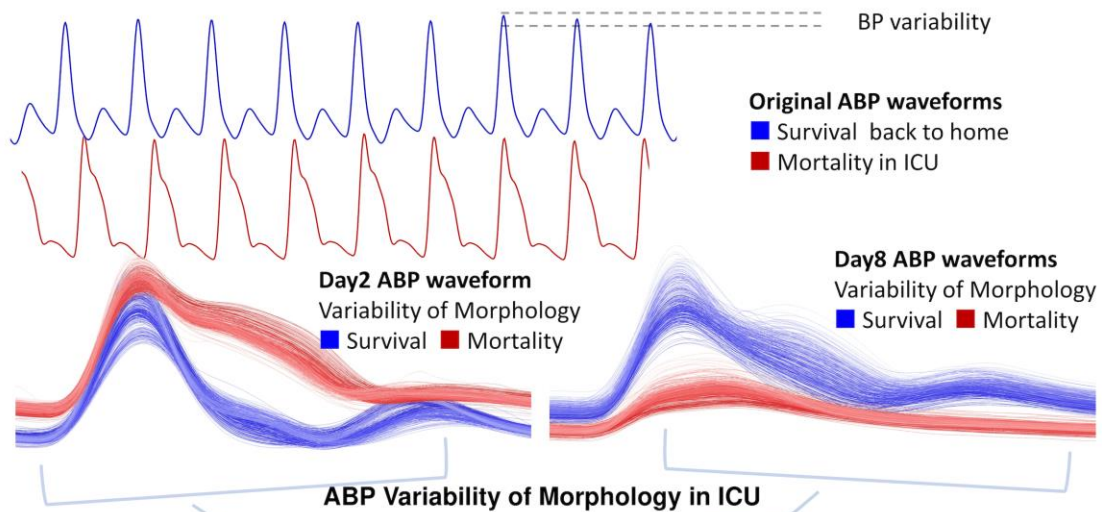
This is a prospective observational cohort study performed in one tertiary academic ICU. We used the *Dynamical Diffusion Map* algorithm, an unsupervised learning algorithm, to quantify the variability of morphology. The quantitative index is summarized every 12 hours. Three clinical outcomes were defined as ICU mortality, in-hospital mortality, and 30-day mortality since ICU admission. We used the daily renewed APACHE II and SOFA scores to represent the disease severity for comparison.

Results:

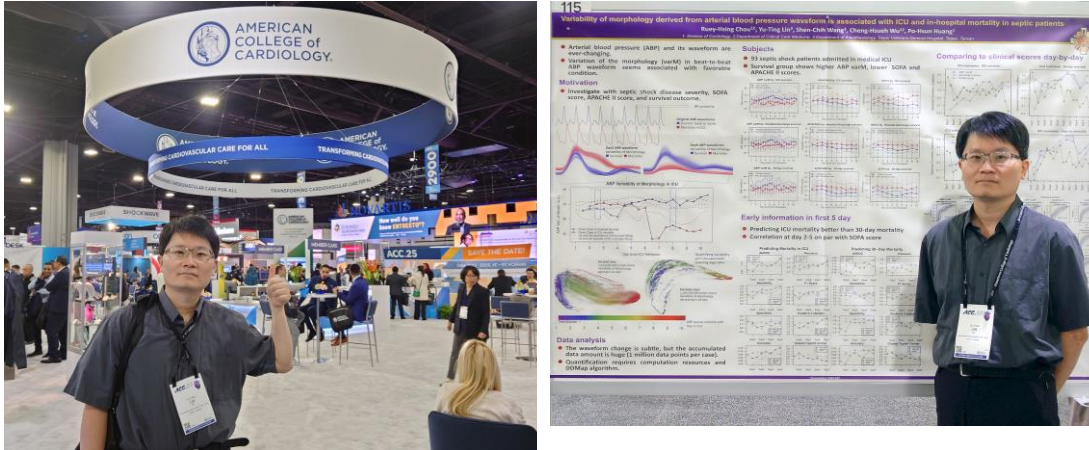
Totally 93 septic patients admitted to ICU were enrolled. Patients of the survival groups from all 3 outcome types present higher variability of morphology in their ABP waveform. The survival groups shows upward trend of variability and downward trends of ABACHE II and SOFA scores in the first 6 days. As a mortality predictor, the ABP waveform variability has greatest performance at day 3. The predictive performance of waveform variability is constantly better than scoring systems in the first 72 hours of ICU stay.

Conclusion:

Upward and higher variability of ABP waveform morphology reflects lower disease severity and better mortality outcomes in septic patients admitted to ICU.



人體生理訊號的波形變化多樣，分析的方法也一直有進展，病生理的機轉也還不明瞭，臨床醫學的變因更是複雜，可以說目前的成果也只是個端倪^{3,4}。另一方面，評估病人的狀況或對癒後進行預測也是臨床上重要的問題，因此這幾個研究方面將來我們仍需要多努力進行。



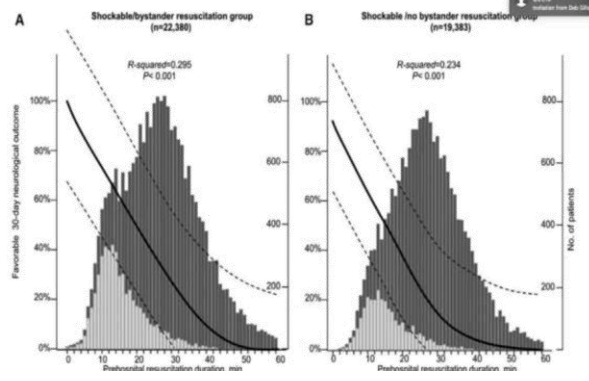
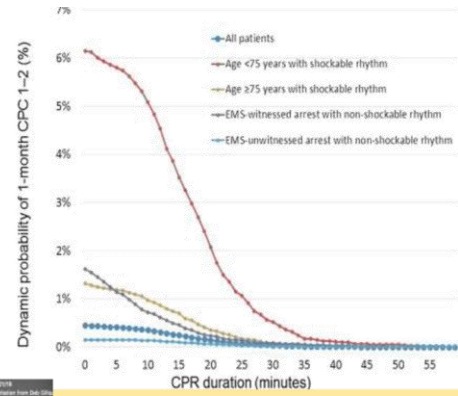
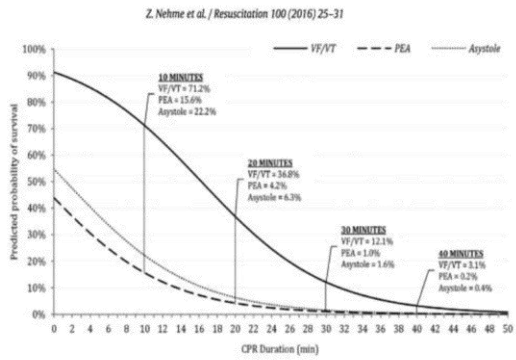
心得及建議

主要的心得有 3 個主題，

1. CPR(ECPR)
2. Targeted temperature management
3. LV unloading in V-A ECMO

CPR(ECPR)

不論在院內還是院外，CPR 的時間愈長，則 outcome 愈差。成因也和 CPR 的 outcome 有關。VF/VT 為最佳，Asystole 與 PEA 則較差。因此將之二分為 shockable rhythm 與 non-shockable rhythm。年齡<75 歲的 shockable rhythm 在 CPR 10 分鐘內有 5% 以上的 CPC 1-2 的癒後，沒有滿足上述條件或是院外 EMS 人員進行的 CPR，相較之下只有不到 2% 的癒後。因此當 CPR 的時間一長，標準的 CPR 流程就顯得無效了。在病因的歸究上，主要是以 coronary artery disease 為主(84%)，因為 acute thrombotic lesion 而需要 CPR。^{5,6}

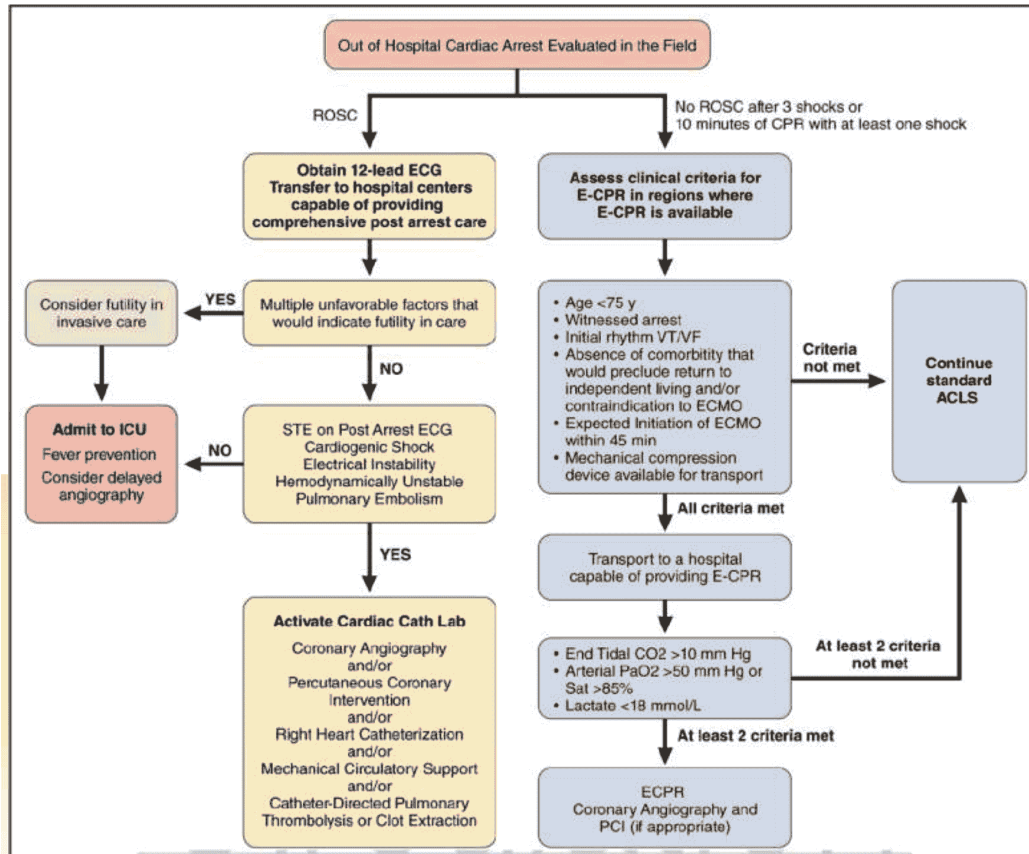


Standard resuscitation strategies are inefficient as the duration of CPR increases. Survival is grim after 30min of CPR even in patients with initial shockable rhythms.

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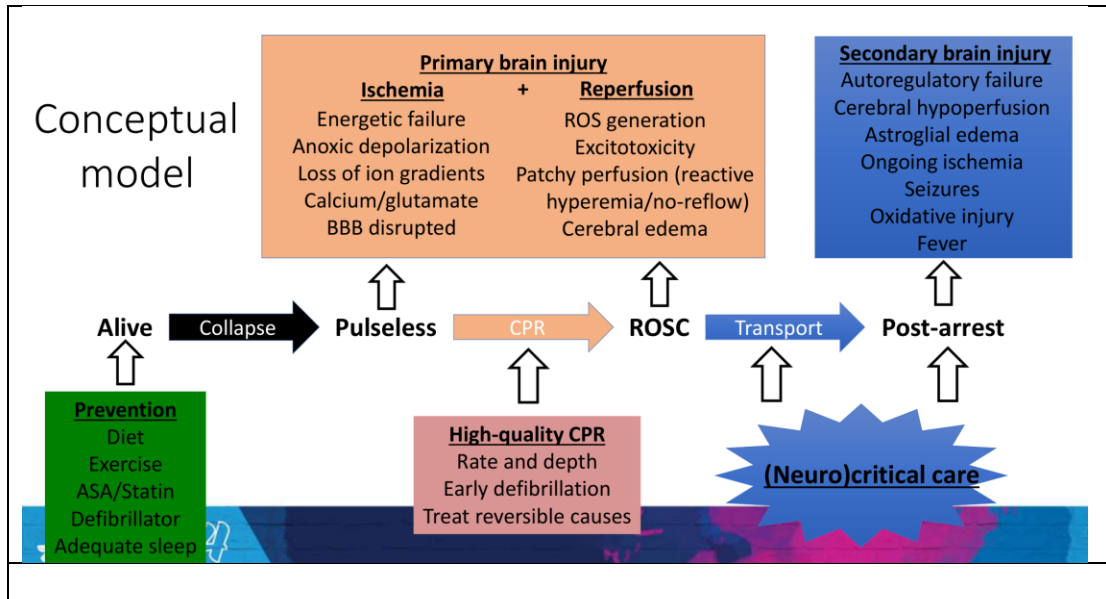
如果以標準的 standard CPR 和 invasive CPR(即 ECMO 參與)相比較，則 invasive CPR 有明顯的 180 天存活優勢。如果以存活為癒後的話，多變數迴歸分析顯示主要有利的因子為 1)initial rhythm “shockable”，2)CPR time <30 分鐘，3)invasive approach，即使用 ECMO。如果就 CPR 的類別去細分，不論是年齡、性別、rhythm、場所時間或 epinephrine 劑量等，皆是支持 ECMO+CPR 較佳。⁷

因此即使在院外 CPR(out of hospital)這樣的場合，ECMO 也在 CPR 流程中占有角色：當 3 次 shock 或超過 10 分鐘的 CPR 且符合適合的條件就可以考慮採用 ECPR 了。⁸



從麻醉醫師的角度來看，最容易連想到的就是開刀房中的 CPR 了，麻醉的情況下會覆蓋一些徵像，如昏痛喘的早期症狀不易察覺，另一方面本院從 20 多年前就開始執行 ECPR 了，只要無法短期間 ROSC 都會即早使用 ECMO 並進行心導管。上面的實證資料也證實我們的臨床常規是合理的。論地域差別的話，可能我們會相較之下有更多的 comorbidity，特別是院內病人是癌症或 organ dysfunction，也有相關的實證顯示這會使得 outcome 不佳(例如 non-shockable rhythm, PEA 等)。另外 anaphylactic shock 也不適合使用 ECMO 和 ECPR 了。這也是臨床上值得考量的。

Targeted temperature management

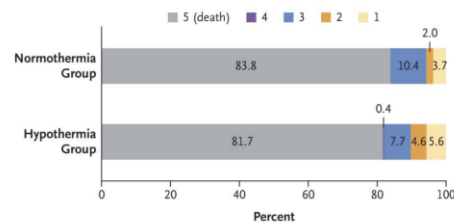


對於 ROSC 的病人，targeted temperature management 的運用對於 outcome 有好處，因為這類病人多會在 CPR 後發燒，但更多的實證顯示降體溫到低於常溫會有好處。從概念上來看，預防不要發生 CPR 就是第一線的工作，是飲食運動作息和公共場所設置 defibrillator。但是當 collapse 發生時就會因為器官失去血氧的供應而出現 primary brain injury，這時能做的工作就是高品質的 CPR，在這個過程中產生的 ischemia 和 reperfusion injury 會造成 neurologic injury，而 CPR 後的 critical care 就會需要面對 autoregulatory failure, cerebral edema, seizure, fever 等病理所形成的 secondary injury。

Temperature management

Mechanism of injury	Effect of hypothermia
1. Primary injury	1. None (unless cooled pre-arrest)
2. ROS generation	2. ROS formation ↓
3. Seizures	3. Seizure threshold ↑
4. Cerebral edema/increased ICP	4. Edema/ICP ↓
5. Ongoing tissue hypoxia	5. Brain metabolism & O ₂ demand (CMRO ₂) ↓

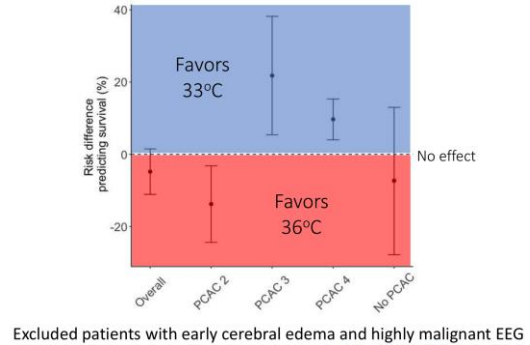
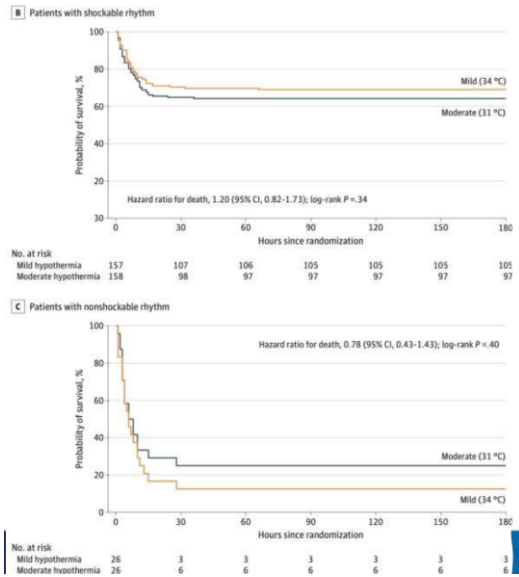
HYPERION



Lascarrou, et al. NEJM. 2019.

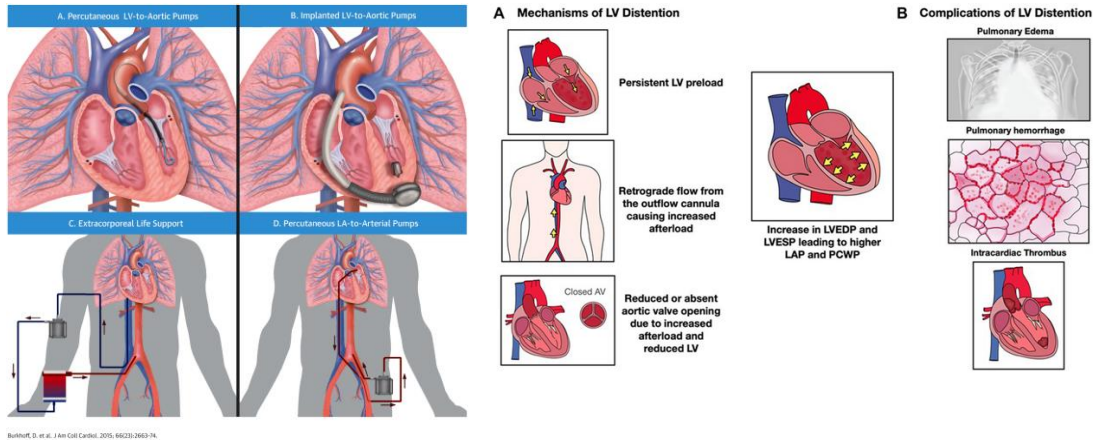
Hypothermia 對於上述的 neurological injury 在學理上都有減輕的作用。實證上也是符合的，HYPERION study 顯示死亡率和嚴重的 neurological

outcome, hypothermia group 都比較少。TTM 執行的時間, 48 小時也比 24 小時有更低的 mortality。但不同的病人族群或有差異, 例如在 out-of-hospital 的 open-label study 中就沒有發現 hypothermia 與 normothermia 的 6 個月 mortality 的差異, 這顯示 CPR 在不同的成因族群有異質性存在。例如: shockable rhythm 的病人, mild hypothermia (34 度) 的存活率較 moderate hypothermia (31 度) 高, 而在 nonshockable rhythm 則相反, moderate hypothermia 比 mild hypothermia 有更好的 survival。

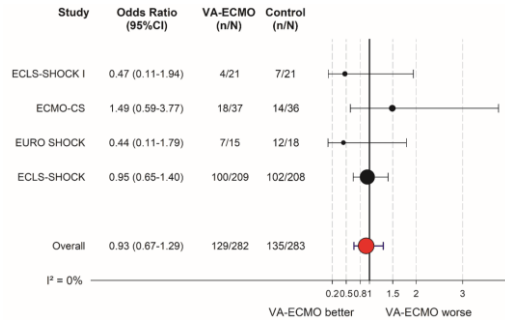
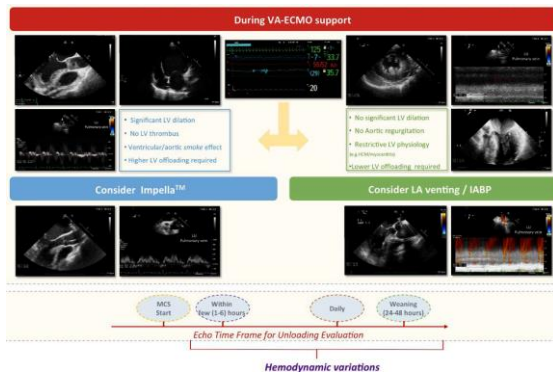


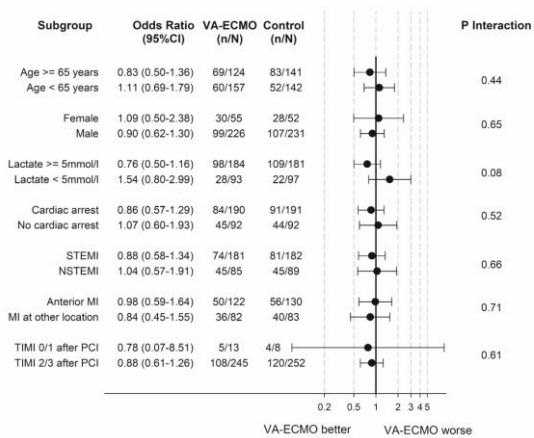
更多的實證顯示, 當 neurologic outcome 可能(PCAC2)較佳時, TTM 維持在 36 度較有利, 而在 neurologic outcome 較差的時候(PCAC3, PCAC4)則 TTM 維持在 33 度較有利。總合來說, 目前 TTM 維持在 33 度-34 度之間有較好的 neurological outcome。⁹

LV unloading in V-A ECMO



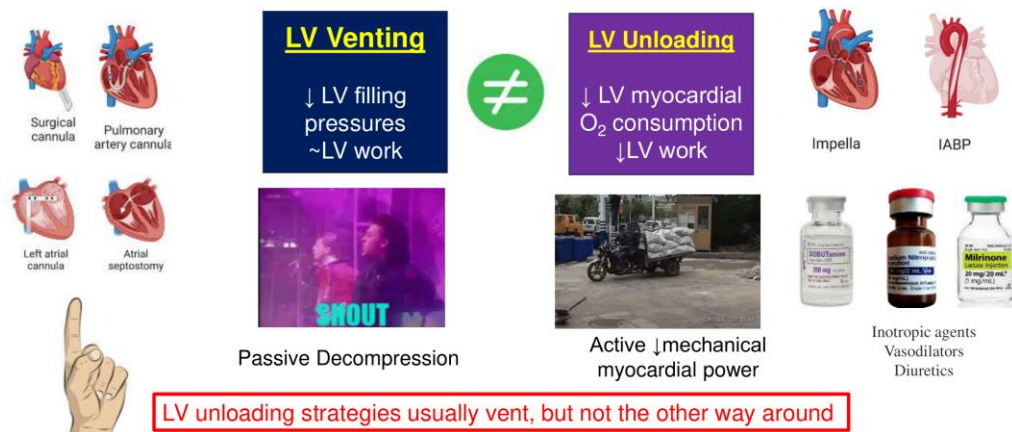
對於 cardiogenic shock 的病人，在 CPR 後使用 mechanical cardiac support device (MCS) 是很常需要的。¹⁰ 這些 device，特別是 ECMO 會逆行性的從 artery 灌注血流，而使得左心漲起來，增加 LVEDP、LVESP，從而使得 LAP 和 PCWP 也壓力上升，造成整個心臟的負擔，不利於 cardiogenic shock 的恢復，也使得肺部也容易出現 pulmonary edema, pulmonary hemorrhage。^{11,12} 這樣的血行狀況也使得血液容易積在心臟裡，造成 thrombus 與後續的風險。對於這樣的狀況，學理上我們需要密集的超音波評估，適當的採用 LA venting、LV unloading 等措施來改善。¹³





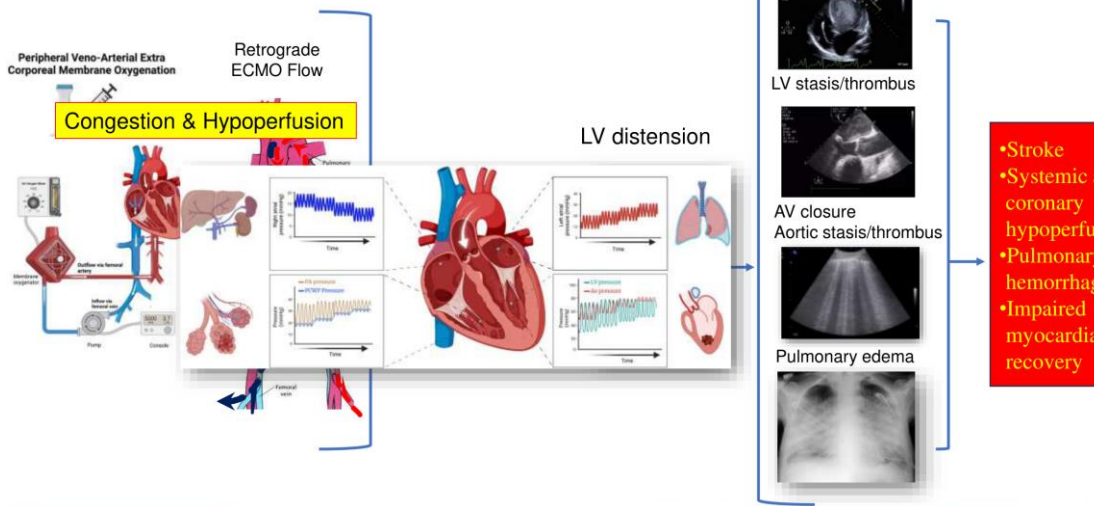
實證顯示，VA-ECMO 在 infarct-related cardiogenic shock 和只有 medical therapy 的 cardiogenic shock 相比，沒有 30-day mortality 的好處，反而還增加出血等風險：「VA-ECMO did not reduce 30-day death rate compared with medical therapy alone in patients with infarct-related cardiogenic shock, and an increase in major bleeding and vascular complications was observed. A careful review of the indication for VA-ECMO in this setting is warranted. (The Lancet 402.10410 (2023): 1338-1346.)」¹⁴

LV Decompression during VA ECMO

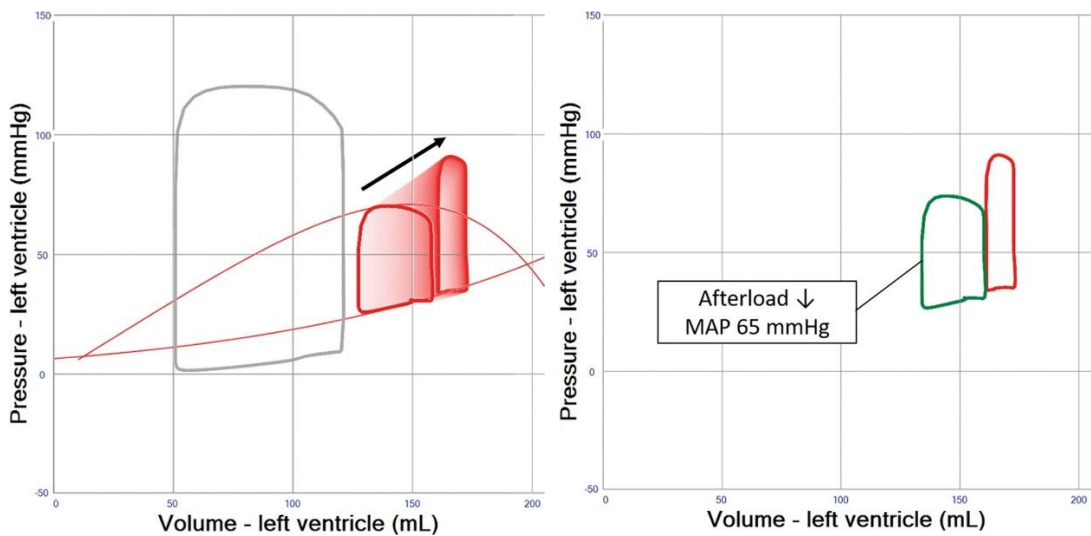


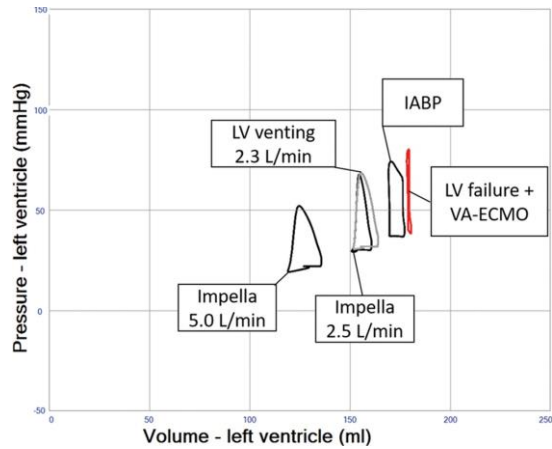
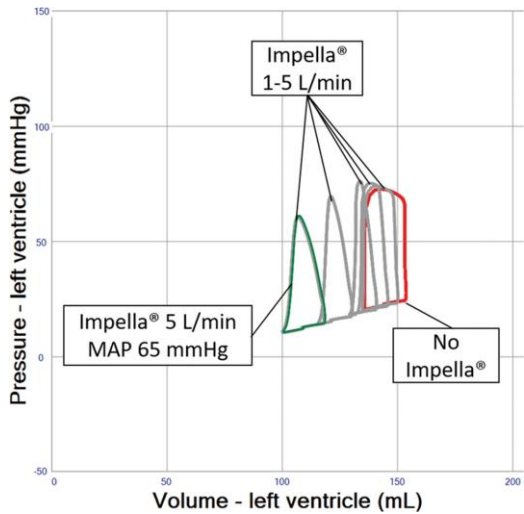
在 VA ECMO 使用中，會需要注意 LV decompression 的需求。概念上，LV venting 不同於 LV unloading。LV venting 減少 LV filling pressure，LV unloading 則希望更積極的減少 LV work 與耗氧等。當我們發現 LV distension，就要預期到 congestion 和 hypoperfusion、中風、肺水腫肺出血等一連串 complication 的發生而及早進行 unloading。^{15,16}

Indications for unloading: Pathophysiology



LV unloading 的相關病生理，可以從模擬的 pressure volume loop 得知。從下圖可以總結出，從正常的生理到當 cardiogenic shock，就會使得 LV pressure volume loop 往 curve 右邊移動，而用上 VA ECMO 後，會更加使得整個 pressure volume loop 右移，在這樣的情況可以用藥物、用 Impella(R) 之類的 device 來緩解，達到 LV unloading 的效果。¹⁷





Meta-analysis 的實證也呈現出 Impella 這樣的 device 對於 LV unloading 可以帶來癒後的好處。關於究竟是等 LV distension 產生再放置 Impella 等時間點的選擇，實證也顯示 2 個小時內放會有更好的 outcome。¹⁸ ECMO+Impella 也產生了新的詞：Ecmella

Left-Ventricular Unloading With Impella During Refractory Cardiac Arrest Treated With Extracorporeal Cardiopulmonary Resuscitation: A Systematic Review and Meta-Analysis*

13 studies, 762 patients

Thevathasan T. CCM, March 2024

A In-hospital mortality

B Good neurologic outcome

Circulation

ORIGINAL RESEARCH ARTICLE

Left Ventricular Unloading is Associated With Lower Mortality in Patients With Cardiogenic Shock Treated With Venocentral Extracorporeal Membrane Oxygenation Results From an International, Multicenter Cohort Study

Circulation. 2020;142:2095-2106.

相較於將 Impella 做為補救的措施，實證更支持在 2 小時內就 active LV unloading。總結起來，Mechanical circulatory support 是有幫助的，而且愈早愈好。

Timing of Active Left Ventricular Unloading in Patients on Venocentral Extracorporeal Membrane Oxygenation Therapy

Study	Active LV unloading before VA-ECMO implantation	Active LV unloading after VA-ECMO implantation
Overall	0.54 [0.33; 0.86]	0.61 [0.34; 1.10]
ECMO+IABP	0.54 [0.33; 0.86]	0.61 [0.34; 1.10]
ECMO+mVAD	0.61 [0.34; 1.10]	0.77 [0.62; 0.95]
IABP	0.77 [0.62; 0.95]	0.98 [0.34; 2.38]
ECMO	0.98 [0.34; 2.38]	0.99 [0.78; 1.35]
No MCS	1.00	1.00
mVAD+mVAD+IABP	4.52 [0.17; 120.26]	

CENTRAL ILLUSTRATION Association Between Timing of Active LV Unloading and 30-Day Mortality

Hazard Ratio

Hours

Active LV unloading before VA-ECMO implantation

Active LV unloading after VA-ECMO implantation

Higher relative risk when used as a bail-out approach

Schrage B, et al. J Am Coll Cardiol Intv. 2023;15(12):1219-1230.

- ↓ mortality & ↓ MV days with active unloading (<2 hrs post ECMO implantation)
- No significant increase in complication rate

Mechanical circulatory support for cardiogenic shock: a network meta-analysis of randomized controlled trials and propensity score-matched studies

Treatment

MCS devices vs. no MCS (All-cause Mortality)

OR 95% CI

ECMO+IABP 0.54 [0.33; 0.86]

ECMO+mVAD 0.61 [0.34; 1.10]

mVAD 0.77 [0.62; 0.95]

IABP 0.98 [0.34; 2.38]

ECMO 0.99 [0.78; 1.35]

No MCS 1.00

mVAD+mVAD+IABP 4.52 [0.17; 120.26]

Favours MCS Favours no MCS

Conclusion: In patients with cardiogenic shock, ECMO+IABP may reduce mortality, while other MCS devices did not reduce mortality. However, this must be interpreted within the context of inter-study heterogeneity and limited certainty of evidence.

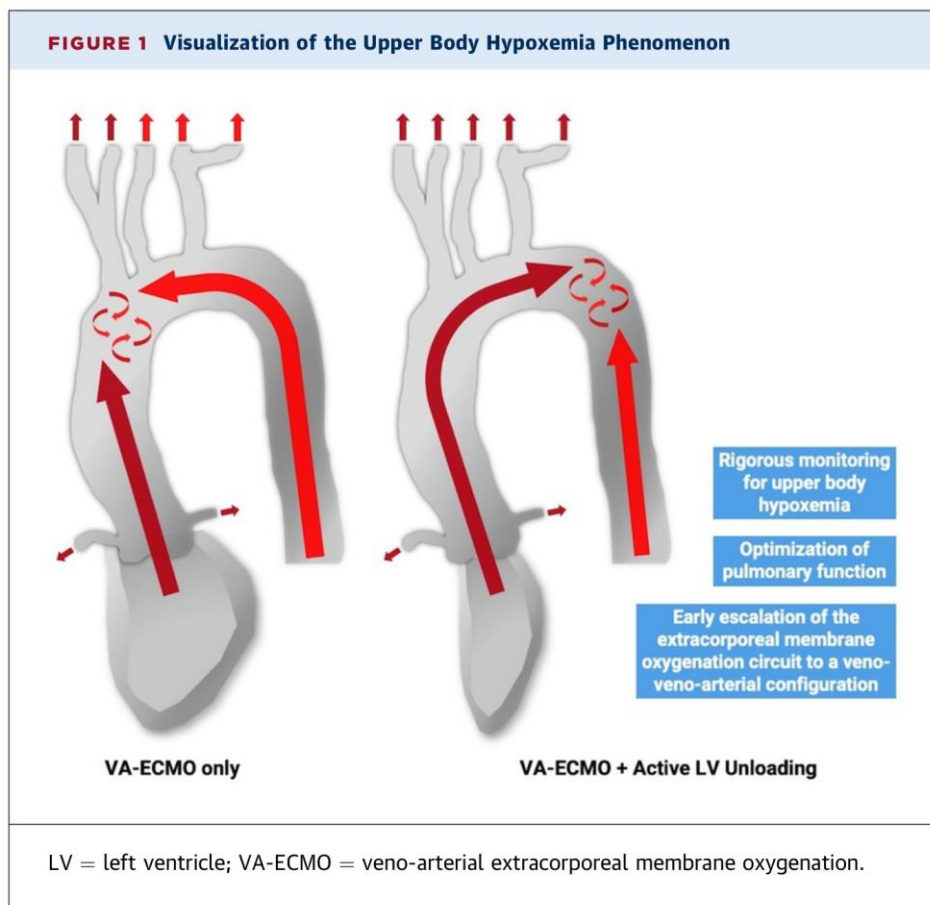
ESC Acute CardioVascular Care 2024

Slide courtesy Guido Tavazzi MD PhD

Intensive Care Med (2024) 50:209-221

ECMELLA(ECMO+Impella)的使用上有個特別的現象，就是當只有 VA-ECMO 時來自 ECMO 的充氧血會從 a-line 逆行灌注到上肢或頭部，但是當加上 Impella 進行

active LV unloading 就可能會出現上肢或頭部反而會 cyanosis，原因在心臟的缺氧血被打出來並進到上半身，造成 upper body hypoxemia。¹⁹



職非常感謝院內、部內長官的支持，心臟內科前輩同事的指引，得以出國開會，一窺廟堂。從心臟醫學的新藥品新醫材的發展可以看到商業資本的投入，許多醫療機構集合研究資源和充足的病人族群才能獲得足夠的實證，因此美國心臟醫學年會此行的心得，使我們麻醉科醫師在開刀房中萬一遇到相似的情況可以做為參考以服務外科的病人。返國後已於麻醉部內晨會(113年5月)口頭報告心得。

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