



2024

VOLUME 24
ISSUE 4

Mobilisation

Mobilisation Matters: Strategies for Efficient Patient Care, *JJ Grunow, N Langer, N Daum, SJ Schaller*

Early Mobilisation - When Evidence Comes to Single Patients, *P Nydahl, L-S Fick, A Hillen, FT Scheffenbichler, SJ Schaller*

Early Mobilisation, Delirium Prevention and Long-Term Cognitive Function, *L Cabrini, O Saleh, G Spinazza, MA Belli*

Early Mobilisation: Just a Fad? *S Garcia-Manzanedo, B Lobo-Valbuena, F Gordo*

Current Controversies in Early Mobilisation in the ICU, *VR Jauregui-Gutiérrez, B Pérez-Martínez, AS Henales-Ocampo, RA Reyes-Monge, OR Pérez-Nieto, E Deloya-Tomas*

Early Mobilisation in ICU: Current Practice and Areas for Improvement, *R Suhail, SM Khorsand*

Early Mobilisation: Movements, Barriers and Complications, *N Canziani, R Cavallari, L D'Andrea, D Goumair*

The ABCs of Physical Therapy for Solid Organ Transplant Patients, *RA Jones Baro, MA Martínez Camacho, A Gómez González, J Delgado Camacho, A Melo Villalobos, DS Lugo García*

Early Mobilisation in Critical Care: Beyond Traditional Limits, *J López Fermín, IS Zamora Guevara, MTG Barragán Castañeda, A Flores Romero, K Vásquez Añas, M Martínez Rojas*

ESICM Webinar – Cardiovascular Management After Surgery

In a webinar at the ESICM Congress, Dr Aretha and Dr Garcia-Alvarez spoke about cardiovascular management after surgery. More specifically, Dr Aretha spoke about the management of post-operative atrial fibrillation, and Dr Garcia-Alvarez spoke about the importance of early application of vasopressin in septic shock patients.

Management of Postoperative Atrial Fibrillation After Cardiac and Major Non-Cardiac Surgery

Post-operative atrial fibrillation (POAF) can be triggered by acute factors, including inflammation, atrial oxidative stress, high sympathetic tone, electrolyte changes and volume overload, to name a few. Incidences of POAF are as high as 62% in certain types of surgery (combined valve surgery and CABG). These incidences can lead to neurological events, including stroke, renal failure, prolonged ICU stays, increased mortality and consequently also increased costs for the hospital (Hindricks et al. 2021; Maesen et al. 2012; Steinberg et al. 2014; Yadava et al. 2016; Zafrir et al. 2018; Lomivorotov et al. 2017; Farmakis et al. 2014; Chyou et al. 2023).

Rate control vs rhythm control

The European Heart Rhythm Association (EHRA) recommends rate control over rhythm control in the acute management of newly diagnosed AF. Haemodynamically stable patients should be assessed for reversible triggers and further be treated with beta-blockers for rate control (Boriani et al. 2019). The 2020 ESC guidelines recommend using beta-blockers, diltiazem or verapamil as a first-choice treatment in AF patients with LVEF \geq 40% for rate control. It is also recommended that patients with LVEF $<$ 40% should be treated with beta-blockers and/or digoxin for rate control. Amiodarone can be used as a last resort

when the heart rate cannot be controlled by first-choice drugs (Hindricks et al. 2020).

According to the EHRA, beta-blockers should be used for rate control in cases of newly onset AF. Specifically, rapid onset and short-acting beta-blockers are preferred if haemodynamic instability is a risk factor (Boriani et al. 2019). Rate control is the preferred approach for ICU and postoperative patients, as the majority will convert to normal sinus rhythm after the resolution of the acute illness. One study showed that 81% of patients with AF reverted to normal sinus rhythm with only rate control treatment (Jones et al. 2020).

Esmolol or Landiolol: Which is the better beta-blocker for treating AF?

While the common beta-blocker used in the post-operative setting is esmolol, esmolol has negative inotropic properties, making its use problematic in patients with haemodynamic instability (Shibata et al. 2012).

Landiolol, which was developed in Japan and has been approved in Europe, is a relatively new beta-blocker with a more favourable pharmacodynamic and pharmacokinetic profile compared to esmolol. While landiolol is also rapid onset and short-acting, it also offers high cardioselectivity – almost eight times higher than esmolol (Krumpal et al. 2017). This is a major advantage as landiolol reduces the heart rate while not interfering with blood pressure. With lower dosing, landiolol is also suitable for patients with impaired

left ventricular ejection fraction (Rapibloc SPC, current version).

According to the proposed algorithm for rate and rhythm control in acute, critically ill or postoperative patients by the European Society of Cardiology (ESC) published in the European Heart Journal Supplements, Volume 24, Issue Supplement_D, in June 2022, esmolol or landiolol should be used for rapid heart rate control (Dan et al. 2022). However, if the patient is haemodynamically unstable, landiolol is the preferred drug due to its more appropriate profile (Johnston et al. 2022).

Early Application of Vasopressin in Septic Shock

Septic shock is mainly characterised by vasoplegia because of the release of inflammatory mediators. The identification of hypoperfusion is key for the survival of these patients to select the most appropriate treatment (Kattan et al. 2022; Ramasco et al. 2024).

Control studies show that early administration of norepinephrine was associated with improved outcomes when treating septic shock. The timing of initiation of norepinephrine should be individualised based on the severity of hypotension (Hamzaoui et al. 2023; Evans et al. 2021).

Norepinephrine or vasopressin?

While the SSC guidelines still recommend using norepinephrine as a first-line treat-

ment, as of 2021, these guidelines advocate adding vasopressin early on as second-line therapy rather than increasing the norepinephrine dose (Evans et al. 2021).

This second-line treatment is recommended because various circumstances in septic shock, including acidosis, hypoxia, hypocalcaemia, relative steroid deficiency and adrenergic receptors being less responsive, can decrease vasopressor effects in norepinephrine. In addition, patients with high levels of norepinephrine have an up to 80% risk of mortality due to the harmful effects of catecholamines (Martin et al. 2015). Furthermore, norepinephrine induces immunoparalysis, which is dysregulation of the immune response, compromising the host defence during sepsis (Stolk et al. 2020).

Dr Garcia-Alvarez suggests early multimodal vasopressors in the treatment of septic shock, which comprises a 'broad spectrum of vasopressors' with several therapeutic targets to achieve decatecholaminisation may be a new approach. With this method, the norepinephrine dose

does not need to be increased thereby improving safety.

Why use vasopressin in septic shock?

Arginine vasopressin (AVP) is a vasoconstrictor with no inotropic effect, a non-catecholamine and has a short half-life (5-15 mins) (Garcia-Alvarez et al. 2023). In Dr Garcia-Alvarez's opinion, the use of vasopressin in septic shock is rationalised by:

1. The fact that there is an AVP deficiency in septic shock.
2. A multimodal strategy sparing catecholamines.
3. A potential nephroprotective effect.
4. The potential improvement of coagulation.

When is the optimal time to introduce AVP?

The SSC guidelines recommend starting vasopressin when the norepinephrine dose is between 0.25 and 0.5 µg/kg/min instead of escalating the norepinephrine

dose (Evans et al. 2021). However, several recent studies showed significant benefits if vasopressin was started within three hours (Brask et al. 2023), at lactate levels <2,3 and/or at norepinephrine doses of <10 µg/kg/min (Sacha et al. 2023).

The response to vasopressin is potentially an indicator of the patient's prognosis. Patients responding to AVP showed lower mortality, more hospital-free days at day 28, and a lower rate of renal replacement therapy (Sacha et al. 2018).

Dr Garcia-Alvarez concludes that it is important to point out that vasopressin is not a rescue treatment but has to be initiated early in the treatment when norepinephrine is at ≥0,25 µg/kg/min to be most effective.

If you want to watch the whole webinar, please visit the webinar library on the ESICM website, or follow this link: <https://mediatheque.cyim.com/mediatheque/media.aspx?mediaId=196721&channel=71460>

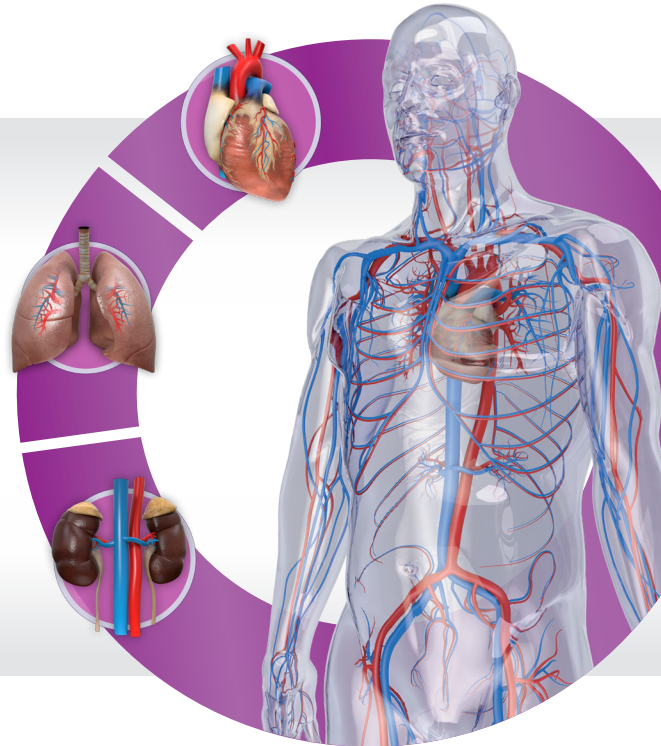
Disclaimer



Point-of-view articles are the sole opinion of the author(s) and are part of the ICU Management & Practice Corporate Engagement or Educational Community Programme.


References

- Boriani G, Fauchier L, Aguinaga L et al. [2019] European Heart Rhythm Association (EHRA) consensus document on management of arrhythmias and cardiac electronic devices in the critically ill and post-surgery patient, endorsed by Heart Rhythm Society (HRS), Asia Pacific Heart Rhythm Society (APHRS), Cardiac Arrhythmia Society of Southern Africa (CASSA), and Latin American Heart Rhythm Society (LAHRS). *Eurpace*. 21(1):7-8.
- Brask AL, Shemanski SM, Barnes TE, Holmes AK [2023] Timing of Vasopressin Addition to Norepinephrine and Efficacy Outcomes in Patients With Septic Shock. *Ann Pharmacother*. 57(5):521-526.
- Chyou JY et al. [2023] Atrial Fibrillation Occurring During Acute Hospitalization: A Scientific Statement From the American Heart Association. *Circulation*. 147(15): e676-e698.
- Dan GA, Dan AR, Ivanescu A, Buzea AC [2022] Acute rate control in atrial fibrillation: an urgent need for the clinician. *Eur Heart J Suppl*. 24(Suppl D):D3-D10.
- Evans L, Rhodes A, Alhazzani W et al. [2021] Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021. *Critical Care Medicine*. 49(11):e1063-e1143.
- Farmakis D, Parissis J, Filippatos G [2014] Insights Into Onco-Cardiology: Atrial Fibrillation in Cancer. *Journal of the American College of Cardiology*. 63(10):945-953.
- García-Álvarez R, Arboleda-Salazar R [2023] Vasopressin in Sepsis and Other Shock States: State of the Art. *J Pers Med*. 13(11):1548.
- Hamzaoui O, Goury A, Teboul JL [2023] The Eight Unanswered and Answered Questions about the Use of Vasopressors in Septic Shock. *J Clin Med*. 12(14):4589.
- Hindricks G et al. [2021] 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. *Eur Heart J*. 42(5):373-498.
- Johnston BW, Chean CS, Duarte R et al. [2022] Management of new onset atrial fibrillation in critically unwell adult patients: a systematic review and narrative synthesis. *Br J Anaesth*. 128(5):759-771.
- Jones TW, Smith SE, Van Tuyt JS, Newsome AS [2021] Sepsis With Preexisting Heart Failure: Management of Confounding Clinical Features. *J Intensive Care Med*. 36(9):989-1012.
- Kattan E, Bakker J, Estenssoro E et al. [2022] Hemodynamic phenotype-based, capillary refill time-targeted resuscitation in early septic shock: The ANDROMEDA-SHOCK-2 Randomized Clinical Trial study protocol. *Rev Bras Ter Intensiva*. 34(1):96-106.
- Krumpl G, Ulc I, Trebs M et al. [2017] Bolus application of landiolol and esmolol: comparison of the pharmacokinetic and pharmacodynamic profiles in a healthy Caucasian group. *Eur J Clin Pharmacol*. 73(4):417-428.
- Lomivorotov VV, Efremov SM, Kirov MY et al. [2017] Low-Cardiac-Output Syndrome After Cardiac Surgery. *J Cardiothorac Vasc Anesth*. 31(1):291-308.
- Maesen B, Nijs J, Maessen J et al. [2012] Post-operative atrial fibrillation: a maze of mechanisms. *Eurpace*. 14(2):159-74.
- Martin C, Medam S, Antonini F et al. [2015]. norepinephrine: Not too much, too long. *Shock*. 44(4):305-9.
- Ramascos F, Aguilar G, Aldecoa C et al. [2024] Towards the personalization of septic shock resuscitation: the fundamentals of ANDROMEDA-SHOCK-2 trial. *Rev Esp Anestesiología Reanim (Engl Ed)*. 71(2):112-124.
- Sacha GL, Bauer SR [2023] Optimizing Vasopressin Use and Initiation Timing in Septic Shock: A Narrative Review. *Chest*. 164(5):1216-1227.
- Sacha GL, Lam SW, Duggal A et al. [2018] Predictors of response to fixed-dose vasopressin in adult patients with septic shock. *Ann Intensive Care*. 8(1):35.
- Shibata S, Okamoto Y, Endo S, Ono K [2012] Direct effects of esmolol and landiolol on cardiac function, coronary vasoactivity, and ventricular electrophysiology in guinea-pig hearts. *J Pharmacol Sci*. 118(2):255-65.
- Steinberg BA, Zhao Y, He X et al. [2014] Management of postoperative atrial fibrillation and subsequent outcomes in contemporary patients undergoing cardiac surgery: insights from the Society of Thoracic Surgeons CAPS-Care Atrial Fibrillation Registry. *Clin Cardiol*. 37(11):7-13.
- Stolk RF, van der Pasch E, Naumann F et al. [2020] Norepinephrine Dysregulates the Immune Response and Compromises Host Defense during Sepsis. *Am J Respir Crit Care Med*. 202(6):830-842.
- Summary of Rapibloc® Product Characteristics, current version.
- Yadava M, Hughey AB, Crawford TC [2016] Postoperative Atrial Fibrillation: Incidence, Mechanisms, and Clinical Correlates. *Heart Fail Clin*. 12(2):299-308.
- Zafir B, Lund LH, Laroche C et al. [2018] Prognostic implications of atrial fibrillation in heart failure with reduced, mid-range, and preserved ejection fraction: a report from 14 964 patients in the European Society of Cardiology Heart Failure Long-Term Registry. *Eur Heart J*. 39(48):4277-4284.

Treating Catecholamine Refractory Hypotension in Septic Shock



-  **Increase mean arterial pressure** in catecholamine refractory septic shock^{1,3}
-  **Reduce Norepinephrine Infusion** while maintaining mean arterial pressure^{1,2}

-  **Increase Chances of Survival** for patients with less severe septic shock (<15 µm/min NE)⁵ and patients at risk of AKI (increased serum creatinine x1.5)⁴

Empressin 40 I.U./2 ml concentrate for solution for infusion. Active substance: Argipressin. **Composition:** One ampoule with 2 ml solution for injection contains argipressin, standardised to 40 I.U. (equates 133 microgram). 1 ml concentrate for solution for infusion contains argipressin acetate corresponding to 20 I.U. argipressin (equating 66.5 microgram). **List of excipients:** Sodium chloride, glacial acid for pH adjustment, water for injections. **Therapeutic indication:** Empressin is indicated for the treatment of catecholamine refractory hypotension following septic shock in patients older than 18 years. A catecholamine refractory hypotension is present if the mean arterial blood pressure cannot be stabilised to target despite adequate volume substitution and application of catecholamines. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. **Undesirable effects: Metabolism and nutrition disorders: Uncommon;** hyponatremia **Unknown:** Water intoxication, diabetes insipidus after discontinuation. **Nervous system disorders: Uncommon;** tremor, vertigo, headache. **Cardiac disorders: Common;** arrhythmia, angina pectoris, myocardial ischaemia. **Uncommon;** reduced cardiac output, life threatening arrhythmia, cardiac arrest. **Vascular disorders: Common;** peripheral vasoconstriction, necrosis, perioral paleness. **Respiratory, thoracic and mediastinal disorders: Uncommon;** bronchial constriction. **Gastrointestinal disorders: Common;** abdominal cramps, intestinal ischaemia **Uncommon;** nausea, vomiting, flatulence, gut necrosis. **Skin and subcutaneous tissue disorders: Common;** skin necrosis, digital ischaemia (may require surgical intervention in single patients) **Uncommon:** sweating, urticaria. **General disorders and administration site conditions: Rare;** anaphylaxis (cardiac arrest and / or shock) has been observed shortly after injection of argipressin. **Investigations: Uncommon;** in two clinical trials some patients with vasodilatory shock showed increased bilirubin and transaminase plasma levels and decreased thrombocyte counts during therapy with argipressin **Warning:** less than 23 mg sodium per ml. **Prescription only. Marketing authorisation holder:** OrphaDevel Handels und Vertriebs GmbH, Wintergasse 85/1B; 3002 Purkersdorf; Austria. **Date of revision of the text:** 02/2022

References: 1. Evans L, Rhodes A, Alhazzani W et al.: Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med (2021) 47:11811247 2. Russell JA: Bench-to-bedside review: Vasopressin in the management of septic shock. Crit Care. 2011; 15(26):119 3. Dünser M.W.: Arginine vasopressin in advanced vasodilatory shock: a prospective, randomized, controlled study; Circulation. 2003 May 13;107(18):23139.17. 4. Gordon A.C. et al.: The effects of vasopressin on acute kidney injury in septic shock. Intensive Care Med 2010; 36:8391. 5. Russel JA: Vasopressin versus Norepinephrine Infusion in Patients with Septic Shock. N Engl J Med 2008; 358:87787

VAS_01_012022_INT



ICU

MANAGEMENT & PRACTICE



icu-management.org  @ICU_Management