ICU
MANAGEMENT & PRACTICE
@ICU_Management
2024
VOLUME 24
ISSUE 3

Patient Monitoring

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Agenda:

1. ECMO in Neonates – An Overview
   (Prof. Dr. Thomas Schaible)
2. How to Perform a Safe Neonatal ECMO Transport
   (Dr. Matteo Di Nardo)
3. Technical and Clinical Considerations for Optimized Cannulation Strategies in Neonatal Care
   (PD Dr. Florian Kipfmüller)
4. Q&A and discussion
   (moderated by Dr. Matteo Di Nardo)

This session is not included in the main event CME/CPD credit.

Find us at booth number 13!

Patient Monitoring

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Patient monitoring in the ICU is critical for providing high-quality medical care. Monitoring involves continuous surveillance of physiological parameters to assess patient condition and detect signs of deterioration promptly. This includes monitoring vital signs such as blood pressure, heart rate, respiratory rate, and body temperature; continuous ECG monitoring, monitoring of respiratory parameters and haemodynamic monitoring.

For patients with neurological conditions, continuous monitoring of electroencephalogram, and variables such as intracranial pressure may be needed for early detection of neurological deterioration. For patients with renal impairment, monitoring urine output, serum creatinine, and electrolyte levels is extremely important. In addition, monitoring parameters such as blood glucose levels, acid-base balance, and lactate levels helps guide interventions to maintain metabolic homeostasis.

Despite advancements in technology and medical practice, patient monitoring presents several challenges. The ICU generates vast amounts of data from various monitoring devices. This data overload can lead to information fatigue and may result in important cues being overlooked. ICU monitoring systems often trigger alarms, many of which may be false or clinically insignificant. Due to the high frequency of these alarms, critical care staff can become desensitised, leading to delayed response or missed critical events.

Patients in the ICU often have complex medical conditions and may require multiple interventions and monitoring modalities simultaneously. Managing and interpreting data from these patients can be challenging. There are also challenges associated with limited availability of resources, such as skilled healthcare personnel, monitoring equipment, and ICU beds. Malfunctions or technical issues with monitoring equipment can disrupt patient monitoring and compromise data accuracy.

Technological advancements, workflow optimisation, staff training, and interdisciplinary collaboration can help address these challenges. Standardised protocols and guidelines can ensure consistency in monitoring practices and facilitate communication among critical care teams. It is equally important to incorporate advanced monitoring technologies, such as wearable sensors, continuous non-invasive monitoring devices, and remote monitoring systems, to provide real-time data on physiological parameters and facilitate early detection of changes in patient status.

In this issue, our contributors discuss how vital signs, cardiac, respiratory, haemodynamic, neurological, temperature, glucose monitoring and other important indicators can help critical care providers make timely and informed decisions in the ICU.

As always, if you would like to get in touch, please email JLVincent@icu-management.org.

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PATIENT MONITORING

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* Pugin, J. et al. Serial Measurement of Pancreatic Stone Protein for the Early Detection of Sepsis in Intensive Care Unit Patients: A Prospective Multicentric Study.

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Pain Monitoring and Management in Intensive Care Unit: A Narrative Review

Pain is defined as an unpleasant sensory and emotional experience. Among patients admitted to the Intensive Care Unit (ICU), severe untreated pain is associated with an increase in mortality, length of hospital stays and worsening in everyday quality of life after hospital discharge. Pain in critically ill patients is more difficult to monitor and manage due to several factors, such as the presence of patients unable to communicate and severe clinical alterations limiting the use of analgesic drugs or the application of analgesic locoregional techniques. We present an extensive narrative review on ICU pain treatment, focusing on tools used to detect this condition and multimodal strategies adopted to reach adequate analgesia.

Introduction

The Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue injury or described in terms of such damage" (Pain 1979).

International PATHOS study (Benhamou et al. 2008), involving 746 European hospitals, highlighted the suboptimal management of postoperative analgesia, supporting the need for improving pain treatment in surgical European wards. This assessment becomes even more critical when considering intensive care unit (ICU) patients. According to recent reports, more than 5 million patients are admitted to ICU in the United States every year. Pain at rest is detected in over half of them, and this number increases to 80% when considering procedural pain (Devlin et al. 2018).

Analgesia in critically ill patients can be very difficult to manage due to several factors, including a limited or a total loss in the patient's ability to communicate, severe emotional distress and important biological alterations that can alter the pharmacokinetic and pharmacodynamic profile of the analgesic drug, restricting their use. Untreated ICU pain is associated with an increase in death, in-hospital delirium, and the development of chronic pain, with a negative impact on the quality of life after hospital discharge (Yamashita et al. 2017). We present an extensive narrative review on ICU pain treatment, focusing on tools used to detect this condition and multimodal strategies adopted to reach adequate analgesia.

Pain Monitoring

Pain is a negative experience for patients in the ICU, where they often undergo invasive and non-invasive procedures (turning, endotracheal suctioning, wound care, central venous catheter and arterial line insertion) (Puntillo et al. 2014). Furthermore, they may experience pain from surgical wounds and underlying conditions. Pain monitoring is important for reducing adverse outcomes such as ICU length of stay and duration of mechanical ventilation (Payen et al. 2007), delirium, post-traumatic stress disorder (PTSD) and increased mortality (Kastrup et al. 2009; Payen et al. 2009). However, assessing pain in critically ill patients can be challenging due to factors such as sedation, mechanical ventilation, and altered consciousness; indeed, all these factors prevent patients from verbally communicating their pain (Ahlers et al. 2008).

According to a 2021 review on pain monitoring in the ICU, pain assessment should take place on admission to the ICU, adopting, even before assessment scales, mnemonic tools useful for focusing on certain aspects of pain. The PQRSTUV mnemonic (Nordness et al. 2021) is frequently used, and it is based on these items:

- Provocative/Palliative factors: Pain cause; pain-relieving strategies;
- Quality: Pain sensation;
- Region: Pain location;
- Severity: Pain intensity;
- Time: Pain duration or temporality;
- Understand: Previous pain experience and known problems;
- Values and preferences for pain treatment.

Pain assessment in the ICU relies on subjective measures such as self-reporting in conscious patients or observational scales for unconscious patients (Devlin et al. 2018). These methods are very useful, but they are limited by several factors, such as subjectivity in evaluation and the need for patient cooperation. There is a high risk of not capturing fluctuations in pain levels over time.

Rating scales commonly used in intensive care are divisible into:

- Unidimensional scales, which measure only intensity, include the Numeric Rating Scale (NRS), Visual Analogue Scale (VAS) and Verbal Rating/Descriptive Scale (VRS/VDS) (Chanques et al. 2022).
- Behavioural scales include Behavioural Pain Scale (BPS), Critical Care Pain Observational Tool (CPOT), Non-Verbal Pain Scale (NVPS) and Pain Assessment in Advanced Dementia (PAINAD).

Numeric Rating Scale

The Numeric Rating Scale (NRS) provides a simple and standardised method for quantifying pain intensity, allowing healthcare providers to assess and monitor pain in ICU patients. This unidimensional scale is a self-reporting scale where individuals rate their pain intensity by selecting a number from 0 to 10 verbally (Puntillo et al. 1997) with:

- 0 = no pain
- 1-3 = mild pain
- 4-6 = moderate pain
- 7-10 = severe pain

The NRS has a maximum acceptable score of 3 (Hamill-Ruth et al. 1999) and can be used across different populations, including adults, children older than eight years and elders, due to its simplicity and ability to provide a quantitative measure of pain intensity (Sessler et al. 2008). The NRS is also the most used scale in cancer patients (Oldenmenger et al. 2017). In the ICU, NRS can also be administered to patients unable to communicate through visual aids (NRS-V), preferably in a large format, making it a usable scale even in lightly sedated patients (Richmond Agitation-Sedation scale (RASS) score greater than -2) (G. Chanques et al. 2022). The pros and cons of NRS are reported in **Figure 1.**

Visual Analogue Scale

Visual Analogue Scale (VAS) is a subjective pain assessment tool that measures both pain intensity and the extent of pain relief (Karcioglu et al. 2018). The VAS is represented as a continuous horizontal (HVAS) or vertical (VVAS) line of 100 millimetres in length with a cursor anchored by verbal descriptors at each end. This pain rating scale has a maximum acceptable score of 30 mm (Ahlers et al. 2008). Patients are asked to mark a point on the line that corresponds to their current level of pain intensity, with one end representing "no pain" and the other end representing "worst pain imaginable" (Jensen et al. 1986). The distance from the "no pain" end to the patient's mark is then measured to quantify pain intensity. The pros and cons of VAS are reported in **Figure 2.**

Verbal Rating/Descriptor Scale

Verbal Rating/Descriptor Scale (VRS/VDS) is a validated pain assessment tool that relies on verbal communication to quantify the intensity of perceived pain (Williamson et al. 2005). This evaluation typically consists of a series of descriptive terms that represent different levels of pain severity. Commonly utilised descriptors include "no pain," "mild pain," "moderate pain," and "severe pain" (Karcioglu et al. 2018). The VRS was the most successful pain scale used in patients with cognitive impairment (Shimoji 2020). The pros and cons of VRS are reported in **Figure 3.**

Several studies have concluded that the most accurate assessment of a patient's pain is a patient's self-report; the recommended and most widely used scales are NRS and VAS, but these scales

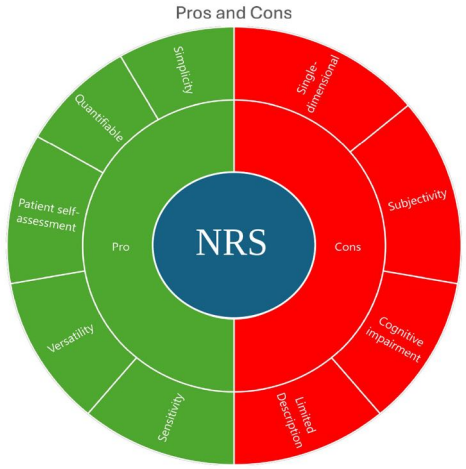

Figure 1. Pros and cons of NRS

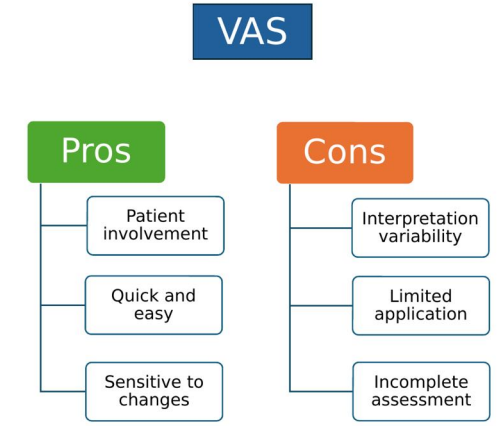

Figure 2. Pros and cons of VAS

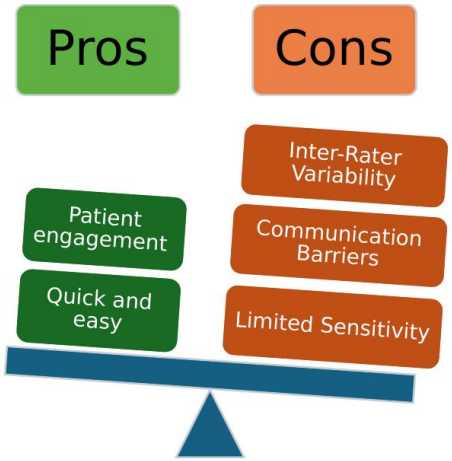

Figure 3. Pros and cons of VAS

can struggle with the reduced consciousness and cognitive impairments often found in ICU patients. However, according to current guidelines, the easiest pain rating scale to use in the ICU, with the highest success rate, and with the best sensitivity and negative predictive value is the NRS (Devlin et al. 2018).

Behavioural Scales

The most cited and utilised scales in intensive care therapies are the Critical-Care Pain Observation Tool (CPOT) and the Behavioural Pain Scale (BPS).

CPOT (Gélinas et al. 2004) is an observational scale that analyses four items:

- facial expression
- body movements
- upper limb muscle tension
- ventilator compliance

Each item is given two points ranging from 2 (no pain) to 8 points (maximum pain). The process of evaluating pain in patients involves several steps:

- establishing a baseline CPOT value while the patient is at rest
- closely monitoring patients' responses during nociceptive procedures
- assessing pain levels before and after administering analgesic agents
- assigning the highest observed CPOT score during evaluation
- scoring each behaviour component of the CPOT, with special attention to muscle tension

This comprehensive approach can ensure a thorough assessment of pain in ICU clinical settings.

BPS (Li et al. 2008) is an observational scale that considers three items:

- facial expression
- upper limb movement
- ventilator compliance

Each item is assigned a score from 1 (no response) to 4 (full response).

When compared with the CPOT scale, the BPS scale showed greater variability in pain score measurement during non-painful procedures like mouthwash and oral care (Gomarverdi et al. 2019). The main limitation of BPS is its consideration of upper limb movement as an integral part of the nociceptive reflex, when in many manoeuvres, this action can be linked only to a non-nociceptive reflex stimulus (Rijkenberg et al. 2017).

Pain Assessment in Advanced Dementia

Another pain assessment scale is **Pain Assessment in Advanced Dementia** (PAINAD), a behaviour-observation tool developed for patients with advanced dementia who lack verbal communication abilities to express pain (Warden et al. 2003). The PAINAD assesses pain through five specific indicators: breathing, vocalisation, facial expression, body language, and consolability. Scores range from 0 to 10, with higher scores indicating more severe pain; in recent years, this tool has also been utilised for sedated or non-verbally expressive patients in ICU.

Nonverbal Adult Pain Assessment Scale

Incorporating patient parameter assessment alongside the previously described items used in CPOT and BPS, we can introduce the Nonverbal Adult Pain Assessment Scale (NVPS) (Azevedo-Santos et al. 2018). The updated version considers five responses:

- facial expression
- activity (movement) guarding
- baseline Respiratory Rate (RR)/SpO_2, ventilator compliance
- physiological parameters (vital signs including blood pressure (BP), heart rate (HR), resting rate (RR).

Each parameter is rated on a scale from 0 to 2, with a total score ranging from 0 (showing no pain) to 10 (indicating maximum pain), with a cut-off of >4 indicating significant pain. The possible misinterpretation of vital signs nonspecific to pain is the main limitation of this scale.

Prospects

The use of innovative technologies in intensive care could improve the pain management of critically ill patients. Some of these technologies such as NOL, ANI, Pupillometer and qNOX can be used for pain monitoring during general anaesthesia in surgery; however, currently, none of these tools has been widely adopted in the ICU because of the lack of strong supporting evidence.

Analgesia Nociception Index

The Analgesia Nociception Index (ANI) is a pain assessment tool that evaluates a single physiological parameter, specifically, the

high-frequency spectrum of heart rate variability (HRV) induced by each respiratory cycle from ECG monitoring of the patient. Data are collected from two electrodes placed on the sternum and axillary midline and analysed by software that provides an index indicating the balance between nociception (low parasympathetic modulation) and analgesia (high parasympathetic modulation). The values provided range from 100 (low level of pain and stress) to 0 (high level of pain and stress). The optimal value that should be obtained during general anaesthesia is between 50 and 70; if less than 50, pain is undertreated; if more than 70, the pain has been overtreated (Shiva et al. 2021). A study on the use of ANI in the ICU to assess pain in critically ill patients during non-painful and painful procedures showed that Mean-ANI (ANIm mean-ANI which is calculated over the previous 4 minutes) is not suitable for ICU patients but Istant-ANI (ANIi calculated in a short period of about 1 minute) is useful for identifying pain in the ICU setting with a negative predictive value of 90% and higher sensitivity in detecting pain during minor procedures (dressing change) than BPS (Chanques et al. 2017). However, ANI can be influenced by several factors, such as age, obesity, disease severity, mechanical ventilation, and anxiety and stress, leading to overestimation or underestimation of pain.

Nociception Level Index

The Nociception Level Index (NOL) is a multi-parameter pain monitoring instrument that provides via a probe placed on a finger a value between 0 and 100, shown on the Pain Monitoring Device monitor (PMD2000 Medasense Biometrics Ltd., Ramat Gan, Israel.) The finger probe includes a sensor to record heart rate (HR), HRV, photoplethysmography wave amplitude, skin conductance level, number of skin conductance fluctuations, skin temperature, and their time derivatives. All these parameters are integrated with a non-linear Random Forest regression technique to provide the NOL index. A value <25 is indicative of pain (Shiva et al. 2021). A study conducted in ICUs to evaluate the NOL's ability to discriminate between nociceptive and non-nociceptive stimuli demonstrated the possibility of exploiting this device to detect pain in critically ill patients, finding confirmation in the parallel measurement made with the CPOT (Shiva et al. 2020). However, there are still few studies on NOL in the ICU to draw any conclusions about the application of this device in this clinical scenario.

qNOX

The qNOX score (ranging from 0 to 99) is a dimensionless proprietary score based on EEG (electroencephalography) and EMG (electromyography) measurements. It is designed to gauge the likelihood of a patient's movement response to a noxious stimulus. The manufacturer suggests that a qNOX score below 40 shows a very low likelihood of a response to a painful stimulus; conversely, a low likelihood with a score between 40 and 60 and a higher likelihood when the score is above 60. The independence of this device from various potential confounders, such as vasoactive drugs, makes this tool conceptually appealing. Boselli et al. (2023) evaluated in a small retrospective study the utility of the qNOX score, particularly concerning its efficacy in discerning responses to noxious stimuli (tracheal suction) among patients under profound sedation and neuromuscular blockade within the ICU setting.

Pupillometry

Pupillometry appears as a valuable adjunctive tool for pain assessment in critically ill patients admitted to the ICU. Recent investigations underscored its reliability, particularly among sedated individuals. Audicana et al. (2023) elucidated the significance of pupillometry in patients exhibiting a RASS score ranging from -4 to -1. They observed that pupillary diameter responses (PDR) offered superior discrimination of heightened pain responses compared to BPS. Moreover, in patients with a more profound sedation level (RASS score 5) (Lukaszewica et al. 2015), pupillary changes were effective in assessing analgesic depth and predicting the presence of pain during invasive procedures performed in the ICU.

Pain Management

The primary goal of pain management in the ICU is to maximise patient comfort. Failing to ensure this important clinical outcome can lead to negative physiological effects, development of chronic pain conditions and increased anxiety and agitation (Lewis et al. 1994; Battle et al. 2013). A thorough evaluation of pain should be paired with a multi-modal treatment strategy, adopting pharmacological and non-pharmacological techniques for alleviating pain (Nordness et al. 2021).

Pharmacological Strategies

For critically ill patients, managing pain typically involves pharmacological approaches, commonly based on the administration of opioids (Devlin et al. 2018; Posa et al. 2020). However, extended use of opioids can result in increased drug tolerance, necessitating larger doses for the same pain relief. Prolonged administration at increasing dosages can also lead to physical dependence and withdrawal symptoms when reducing opioid use. Moreover, such prolonged opioid consumption may contribute to the onset of chronic pain and induced hyperalgesia (Chu et al. 2008; Puntillo et al. 2016). To counteract these risks, an appropriate use of opioids, with an adequate plan of opioid rotation and coadministration of nonopioid analgesics is required. A tiered pain management strategy is also recommended, analogous to the approach the World Health Organization suggests for cancer patient care (Ventafridda et al. 1985). Current guidelines also recommend the strategy of analgosedation, which prioritises pain management before starting sedation therapy, using sedation only if necessary (Pun et al. 2019).

Routes Of Administration

The reasons for ICU admissions are diverse, primarily categorised into surgical and medical patients, each presenting with various states of dysfunction, including cerebral, cardiovascular, renal, and respiratory issues. The administration of drugs must always consider potential risks, with adjustments in route and

dosage tailored to the individual patient's needs. Intravenous (IV) administration is preferred over intramuscular or subcutaneous routes due to the unpredictable bioavailability associated with the last two methods (Devlin et al. 2018; Chou et al. 2016). However, alternative methods like regional analgesia or patient-controlled analgesia (PCA) may be selected depending on the patient's state of consciousness and the nature of their pain, such as postoperative discomfort (Levy et al. 2011). These choices are guided by the principle of multimodal analgesia, with the goal of reducing opioid consumption (Wick et al. 2017).

Opioid Analgesics

Opioids alleviate pain by acting on specific areas of the brain (cortex, thalamus, hypothalamus, locus coeruleus, amygdala, and periaqueductal grey matter) as well as the spinal cord and the membranes of peripheral nerves (Martyn et al. 2019). Opioid receptors, like Mu and Delta receptors (MORs and DORs), are both Gαi/o-coupled GPCRs and are activated by opioids. This activation leads to a reduction in neuronal activity and synaptic transmission. The main characteristics of opioids used in ICU are reported in **Table 1**.

Morphine is poorly lipophilic, and like all opioids, this drug undergoes primary metabolism in the liver, with metabolites being expelled through urine. Morphine has an onset of action of 5 to 10 minutes with a half-life of 4 hours and several active metabolites that can accumulate in the case of renal failure. To prevent this effect, the maintenance dose of morphine must be reduced by 50% in this category of patients (Aronoff et al. 2007). Morphine also stimulates the release of histamine, which can cause hypotensive events (Lambert et al. 2023). However, the release of histamine-induced by morphine does not cause bronchoconstriction (Eschenbacher et al. 1984).

Fentanyl is 600 times more lipid soluble compared to morphine. This characteristic enables fentanyl to have a rapid onset of action, approximately 1 minute, and a relatively short half-life ranging from 0.5 to 1 hour. Bolus administration could be useful in the management of procedural pain (Siffleet et al. 2007; Robleda et al. 2016). The metabolism of fentanyl occurs in the liver, leading to the production of inactive metabolites that are then excreted. This metabolic pathway makes fentanyl a more suitable option for patients with renal insufficiency (Davison et al. 2019). Despite its advantages, the use of fentanyl requires careful monitoring. Its administration can result in possible adverse effects, including respiratory depression (Dahan et al. 2010).

Hydromorphone is considered 5 to 10 times more potent than morphine (Felden et al. 2011). Its onset of action occurs within 15 to 30 minutes, and it has a half-life ranging from 2 to 3 hours. While it may require dose reduction in patients with renal impairment, hydromorphone is a beneficial option for dialysis patients since hydromorphone-3-glucuronide is removed during haemodialysis (Davison et al. 2008).

Remifentanil is an extremely lipophilic drug. This characteristic enables it to have a rapid onset of action, approximately 1 minute, and an extremely short half-life ranging from 12 to 30 minutes (Kapila et al. 1995). It is administered as a continuous infusion. Since remifentanil is metabolised by nonspecific esterase in the plasma without involving the liver or kidneys, no dose adjustment is required for patients with renal or hepatic insufficiency. This feature, combined with its rapid onset and offset, positions remifentanil as the preferred sedative-analgesic agent in ICU, allowing frequent neurological assessments and reducing the time to extubation (Dahaba et al. 2004; Breen et al. 2005).

Opioids	Route of administration	Dosage	Characteristics	Half-life
Morphine	IV, IM, PO, SC	0.1 mg/kg	Poor lipophilic	4 hours
Fentanyl	IV, IM, PO, SC	2-5 mcg/kg	High lipophilic	1 hour
Hydromorphone	IV, IM, PO, SC	0.08 mg/kg	Poor lipophilic	2.5-3 hours
Remifentanil	IV, CI	Starting from 0.02 mcg/kg/min	Extremely lipophilic	12 to 30 minutes

Table 1. Main opioids used in the ICU. *IV intravenous, IM intramuscular, PO per os, SC subcutaneous, CI continuous infusion*

Non-Opioid Analgesics

Acetaminophen's pain-relieving effect primarily occurs through the activation of descending serotonergic pathways. However, there is some discussion regarding the main mechanism of action, which is believed to involve the suppression of prostaglandin synthesis (Anderson et al. 2008). This drug is indicated in the treatment of fever and mild pain, and it should be used as an adjunct to opioids to reduce pain intensity and opioid consumption for pain management in critically ill adults (Devlin et al. 2018). The recommended dosing is 1g every 6 hours IV with a maximum dose of 4g. Acetaminophen's dose adjustment should be applied for patients with mild to moderate hepatic insufficiency or body weight less than 50 kg, with no reduction for renal impairment. In the setting of ICU, a prospective observational study (Cantais et al. 2016) demonstrated a correlation between IV acetaminophen administration and development of hypotension in half of the treated patients, with the need of therapeutic intervention in one third of observed episodes.

Nonsteroidal Anti-Inflammatory Drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs) non-selectively inhibit cyclooxygenase, playing a key role in reducing inflammation. However, this mechanism also poses a risk of adverse events, particularly affecting the gastrointestinal tract and causing renal impairment.

Ketolorac - dosing 30 mg IV, maximum 120 mg per day for up to 5 days.

Ibuprofen - dosing 400-600 IV, maximum 3.2 g/day.

NSAIDs are indicated in the short-term treatment of moderate pain and as adjuncts in multimodal therapeutic regimens, with the goal of reducing opioid consumption.

Ketamine

The recommended dosage for ketamine is 0.5 mg/kg bolus followed by a 1-2 mcg/kg/min infusion (Cook et al. 2020). This drug provides strong pain relief through its action of blocking N-methyl-D-aspartate (NMDA) receptors, thereby reducing the release of glutamate and attaching to sigma-opioid receptors (Nadeson et al. 2002). Low-dose ketamine is advocated as a supplementary treatment alongside opioid therapy, aimed at minimising opioid intake in adults who have undergone surgery and are admitted to the ICU. A recent meta-analysis showed that ketamine had better analgesic effects in the early treatment of acute pain, while morphine maintained more durable effects (Juan Guo et al. 2024).

Neuropathic Pain Medications

The use of neuropathic pain medications, in addition to opioids for neuropathic pain management, is recommended by the Society of Critical Care Medicine (SCCM) guidelines (Devlin et al. 2018).

Their analgesic effects are mainly due to blocking calcium channels which reduce the release of excitatory neurotransmitters, dampening pain-enhancing signals from the brain and reducing inflammation with a positive impact on the emotional aspects of pain (Chincholkar et al. 2018).

Gabapentin – dosing oral - initially 100mg 3 times per day - maintenance 900 to 3600mg per day in three different administrations.

Pregabalin – dosing oral: initially 75mg – maintenance 150 to 300 twice per day.

Carbamazepine – dosing oral: 200 to 400 mg/day in 2-4 divided doses – maintenance 600 to 800 mg/day in 2-4 divided doses. Maximum 1.2 g/day.

Non-Pharmacological Strategies

A recent review by Nordness et al. (2021) emphasises the significance of nonpharmacological strategies, underlining four key points that are also reflected in the SCCM guidelines (Devlin et al. 2018).

Non-pharmacological interventions include a range of practices, from massage and cold therapy to music/sound therapy and relaxation techniques. These methods aim not only to alleviate the physical aspects of pain but also to address the emotional and psychological components. For example, massage therapy can provide relief and comfort to patients, potentially reducing the need for higher doses of pain medications (Mitchinson et al. 2007). Similarly, music and sound therapy can offer a soothing and distracting influence, which may help in reducing pain perception (Jaber et al. 2007).

These strategies offer several benefits, including minimising the reliance on pharmacological interventions, which can have side effects and contribute to issues such as opioid dependence.

Employing such approaches can contribute to achieving better pain management outcomes, enhancing patient comfort and facilitating recovery. As the field continues to evolve, further research and integration of nonpharmacological pain management strategies will be essential in improving care for ICU patients.

Locoregional Techniques

Enhanced Recovery after Surgery (ERAS) protocols supported the use of multimodal strategies to manage postoperative pain, including not only pharmacological approaches but also locoregional techniques. Locoregional blocks are a fundamental part of most analgesic ERAS protocols for surgery (Mancel et al. 2021). Thoracic epidural catheter placement is the gold standard approach to manage severe abdominal and thoracic pain after laparotomic surgical procedures. This technique, although effective, may not be used in critically ill patients due to several factors, including the risk of serious central neuraxial infections, the presence of sepsis, haemodynamic instability, and haemostatic abnormalities. The diffusion of ultrasound-guided manoeuvres allowed the application of several locoregional techniques also in critically ill ICU patients. Fascial ultrasound-guided blocks were demonstrated to be safe and effective for pain management of the abdomen (Tranversus Abdominis Plane-TAP- block) (Niraj et al. 2009) and thorax (Erector Spinae Plane-ESP -block) (Gursoy et al. 2020).

However, all these blocks should be performed only by clinicians with a high level of experience. Future large randomised controlled trials are necessary to better define the role of locoregional procedures in achieving pain control among ICU patients.

Conclusion

Pain in ICU patients is a complex and multifactorial condition, very difficult to detect and manage. Inadequate ICU pain management is associated with an increase in mortality and morbidity during hospital stay and severe worsening in the everyday quality of life after discharge. Pain should be considered as important as other vital parameters, and analgesia should be managed as other life-support systems. The definition of institutional standardised protocols, including tools to detect and monitor pain and multimodal therapeutic analgesic strategies, should be mandatory in ICU patients' management.

Conflict of Interest

None.

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How and Why We Should Monitor Dyspnoea in Mechanically Ventilated Patients

Dyspnoea is among the worst suffering that a human being can experience. Because mechanically ventilated patients are strongly exposed to high dyspnoea intensity, it is important that clinicians monitor dyspnoea in this population. Relieving dyspnoea in patients is a human right.

Suffocating, not getting enough air or the feeling that breathing is difficult or even abnormal is among the worst suffering that a human being can experience. Because mechanically ventilated patients are at high risk of experiencing dyspnoea, the European Respiratory Society (ERS) and the European Society of Intensive Care Medicine (ESICM) decided a statement paper was required.

Recently, a multidisciplinary task force, with members from the ERS and the ESICM, including specialists in intensive care, respiratory intensive care, pulmonology, respiratory physiology, psychiatry, neurophysiology, and palliative care, together with a patient representative of the European Lung Foundation, addressed key issues related to the clinical problem of dyspnoea in critically ill mechanically ventilated patients. In addition to a systematic database search of medical literature, a patient-centred literature review was performed to explore the experiences of patients who had suffered dyspnoea while being mechanically ventilated for an acute illness. The manuscript was published in the *European Respiratory Journal and Intensive Care Medicine* (Demoule et al. 2024a; Demoule et al. 2024b).

Task Force Members first agreed on a new definition of dyspnoea, which is the symptom that conveys "an upsetting or distressing experience of breathing awareness". Previously, dyspnoea was defined by the American Thoracic Society as "a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity" (Parshall et al. 2012). Although clear, this definition was sophisticated and not operational enough at the bedside, and the word "discomfort" was probably too weak to describe the intensity of the distress/suffering associated with dyspnoea in invasively mechanically ventilated patients.

Clearly, reviewing the literature shows that dyspnoea is a frequent issue in invasively mechanically ventilated patients. In this population, the occurrence or intensity of dyspnoea has been investigated in approximately 50 studies, retrospective or prospective. Although these studies are extremely heterogeneous in terms of the design, it can be estimated that the median prevalence of mechanically ventilated patients who experience is approximately 45%. When present, dyspnoea ranges from 40 mm to 60 mm on a scale from zero (no dyspnoea) to 100 (worst imaginable dyspnoea). Altogether, these data show that dyspnoea in critically ill patients is frequent and rated as severe by patients. A similar level of pain would certainly be judged unacceptable by caregivers and would trigger an immediate response.

Why it is Essential to Monitor Dyspnoea at Bedside

In mechanically ventilated patients, dyspnoea has many consequences, which may occur either during the intensive care unit (ICU) stay or be delayed (**Figure 1**).

The first reason we should monitor dyspnoea is that it causes immediate respiratory suffering. Although it shares many similarities with pain, dyspnoea can be far worse than pain in that it is consistently associated with the fear of dying. The patient-centred literature review that the Task Force performed showed not only that dyspnoea is a terrifying sensation (*"It's hell. Not getting air"* (Karlsson et al. 2012)) but also that dyspnoea is clearly associated with the fear of dying (*"I felt like I was dying and didn't get any air"*) (Samuelson 2011), (*"I often thought about death while I was attacked by dyspnoea"*) (Shih and Chu 1999). In addition, mechanically ventilated patients with dyspnoea are more likely to present with anxiety than non-dyspnoeic patients (71% vs. 24%) (Schmidt et al. 2011). Dyspnoea and anxiety are linked, so dyspnoea can generate or amplify anxiety, which in turn may amplify dyspnoea. Monitoring dyspnoea and reducing its intensity may, therefore, help reduce the terrible experience associated with this symptom.

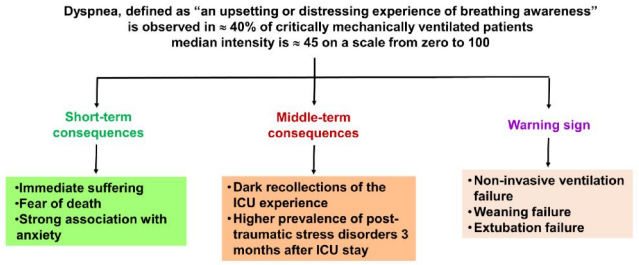

Figure 1. Consequences of dyspnoea

Second, in addition to these short-term outcomes, dyspnoea contributes to the severe neuropsychiatric sequelae of ICU. Survivors of an ICU stay often carry extremely dark respiratory recollections of the experience of being mechanically ventilated, which may persist for several years. Among mechanically ventilated COPD patients, the worst recollection of ICU stay is poor sleep, after which comes suffocation, which is observed in 55% of patients (de Miranda et al. 2011). The combination of a distressing threat to life and a feeling of helplessness may generate post-traumatic stress disorder, which is observed in approximately 20% of ICU patients (Righy et al. 2019). In mechanically ventilated patients, the proportion of post-traumatic stress disorder 90 days after ICU admission is higher in those who experience dyspnoea (29%) than in those who did not (13%), and the repetition of dyspnoea episodes is strongly associated with post-traumatic stress disorder. Monitoring dyspnoea could help reduce the severe neuropsychiatric sequelae that dyspnoea contributes to generating.

The third reason we should monitor dyspnoea is because it is a warning sign. Indeed, dyspnoea is likely to result from a load capacity imbalance of the respiratory system. For instance, a higher level of dyspnoea seems to be associated with a higher risk of weaning failure (Decavèle et al. 2022a). During a spontaneous breathing trial, a high level of dyspnoea is associated with a higher level of failure (Bureau et al. 2022). In intubated patients, persistent dyspnoea, despite optimisation of ventilator settings, is associated with delayed extubation (Schmidt et al. 2011). Finally, once patients are extubated, a high level of dyspnoea, assessed two hours after extubation, is associated with a higher risk of post-extubation acute respiratory failure with subsequent need for re-intubation (Dres et al. 2021).

The Invisibility of Dyspnoea or Why Clinicians Often Ignore it in Patients

Dyspnoea is a symptom (as opposed to a physical sign) that places a very strong emphasis on self-reporting. The observation of signs of respiratory distress (e.g., tachypnoea and laboured breathing) may indicate the presence of dyspnoea, but these findings may be blunted by sedative or paralytic medications in mechanically ventilated patients. The inability to verbally or physically report a symptom does not mean it is not present, as clearly stated about pain (Raja et al. 2020). Data from many studies suggest that, for various reasons, the prevalence, intensity and impact of dyspnoea are underestimated by caregivers when assessing mechanically ventilated patients.

First, patients are not asked. There is a low level of awareness of this symptom within the ICU community. Actually, as opposed to pain, which each caregiver has experienced, very few caregivers have experienced dyspnoea (e.g. those with a chronic respiratory disease or who got near drowning) (Decavèle et al. 2022b). In addition, there are no guidelines that recommend routinely assessing dyspnoea in ICU patients. Finally, caregivers report that relieving dyspnoea presents a greater challenge than relieving pain (Gentzler et al. 2019).

Second, critically ill mechanically ventilated patients are frequently unable to self-report dyspnoea. The endotracheal limits vocal self-report of dyspnoea. In addition, other factors such as sedation, delirium or poor language may impair their ability to self-report dyspnoea. However, being noncommunicative does not mean that a patient is not suffering from dyspnoea. It only means that the patient cannot report it reliably. In other terms, the inability to communicate intentionally and reliably does not negate the possibility of experiencing dyspnoea.

Third, physicians, respiratory therapists and nurses fail to accurately assess dyspnoea based on their own observation of the patients they are managing (Binks et al. 2017; Gentzler et al. 2019; Haugdahl et al. 2015). For this reason, dyspnoea in mechanically ventilated patients may be characterised as "invisible". In one study, where patients attributed a score of 50mm to dyspnoea on a visual analogue scale (VAS) from 0 to 100 mm, nurse and physician estimations were 20 mm (Haugdahl et al. 2015). The degree of underestimation increases as the patient's rating rises (Binks et al. 2017).

How to Detect Dyspnoea in Mechanically Ventilated Patients

Like pain, the assessment of dyspnoea is based on self-report, which requires the patient to be communicative. In noncommunicative patients, observation scales or physiological markers can be used as dyspnoea surrogates.

Self-report of dyspnoea in communicative patients

As is the case with pain (Devlin et al. 2018), in order to self-report dyspnoea, the patient must be able to interpret sensory stimuli, pay attention to the clinician's instructions, concentrate to formulate a dyspnoea self-report and be able to communicate in some way. Unfortunately, less than 50% of patients receiving invasive mechanical ventilation are able to reliably self-report their symptoms (Demoule et al. 2022; Puntillo et al. 2010). Before searching for dyspnoea, it is therefore essential to assess whether a patient is able to reliably self-report a symptom.

A. RDOS

Variables	0 points	1 point	2 points
1 - Heart rate (beats/min)	< 90	90-109	≥ 110
2 - Respiratory rate (breaths/min)	≤ 18	19-30	> 30
3 - Restlessness: nonpurposeful movements	None	Occasional, slight movements	Frequent movements
4 - Paradoxical breathing pattern: abdomen moves in on inspiration	None		Present
5 - Use of neck muscles during inspiration: rise of clavicle during inspiration	None	Slight rise	Pronounced rise
6 - Grunting at end inspiration: guttural sound	None		Present
7 - Nasal flaring: involuntary movement of nares on inspiration	None		Present
8 - Facial expression or fear	None		Eyes wide open, facial muscle tense, brow furrowed, mouth open, teeth together

B. IC-RDOS

Variables	Score
0 -	3.3
1 - Heart rate (beats/min)	+ (Heart rate) / 65
2 - Use of neck muscles during inspiration *if present* *if absent*	 + 1 - 1
3 - Paradoxical breathing pattern *if present* *if absent*	 + 1 - 1
4 - Facial expression of fear *if present* *if absent*	 + 1 - 1
5 - Oxygen supplemental *if present* *if absent*	 + 0.7 - 0.7

C. MV-RDOS

Variables	Score
0 -	3.3
1 - Heart rate (beats/min)	+ (Heart rate) / 65
2 - Use of neck muscles during inspiration *if present* *if absent*	 + 1 - 1
3 - Paradoxical breathing pattern *if present* *if absent*	 + 1 - 1
4 - Facial expression of fear *if present* *if absent*	 + 1 - 1
5 - Respiratory rate (breaths/min)	+ (Respiratory rate) / 50

Figure 2. Calculation of the A Respiratory Distress Observation Scale (RDOS), B intensive care RDOS (IC-RDOS) and C the mechanical ventilation RDOS (MV-RDOS) (Demoule et al. 2024a)

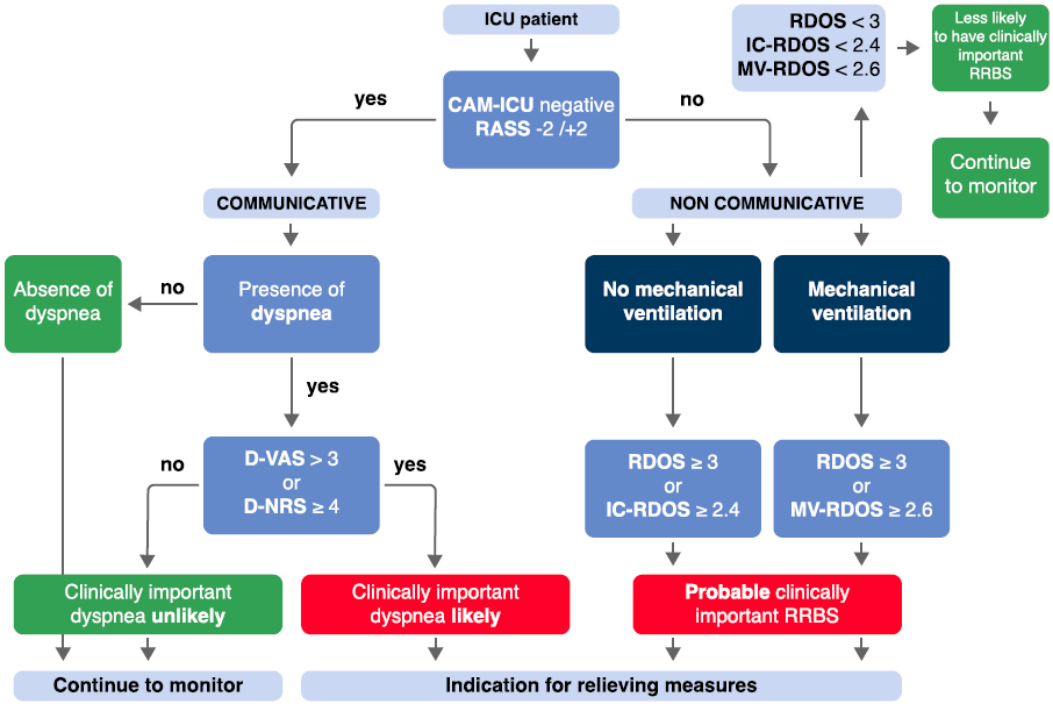

Figure 3. Patient bedside dyspnoea assessment algorithm in the intensive care unit (ICU) setting (Demoule et al. 2024a). *RASS* Richmond Agitation and Sedation Scale, *CAM-ICU* Confusion Assessment Method for ICU, *D-VAS* dyspnoea visual analogue scale, *D-NRS* dyspnoea numerical rating scale, *RDOS* Respiratory Distress Observation Scale, *ICRDOS* intensive care RDOS, *MV-RDOS* mechanical ventilation RDOS, *RRBS* respiratory-related brain suffering

The following approach is usually used to detect the presence of dyspnoea; the caregiver may employ dichotomous trigger questions, such as *"Is your breathing comfortable?" Do you feel breathless? Is your breathing difficult? Are you getting enough air?"* Consistency between the answers reinforces the conviction that self-report is reliable in a given patient. The last step is then to evaluate the intensity of dyspnoea. Although more than 40 tools are available to quantify the intensity of dyspnoea (Mularski et al. 2010), none are ideal for critically ill patients. The simplest way is probably to use a 0–10 numerical rating scale (NRS), which consists of determining, either verbally (asking between 0 and 10) (Morris et al. 2007) or visually (pointing a finger/mark on the 0–10 scale), which value corresponds to the patient's dyspnoea intensity (Gift and Narsavage 1998). An alternative is the modified Borg category–ratio (0–10) scale that consists of verbal descriptors linked to specific numbers (Burki 1987).

Inference of dyspnoea in noncommunicative patients

Observation scales have been initially developed to detect dyspnoea in noncommunicative patients (Campbell et al. 2017). They are based on observable signs of respiratory distress correlated with dyspnoea. The Intensive Care - Respiratory Distress Observation Scale (IC-RDOS) is a five-item ordinal scale, which infers the presence of dyspnoea based on three components: respiratory (use of neck muscles, paradoxical motion of the abdomen, need for oxygen), vegetative (heart rate) and emotional (facial expression of fear) (Decavèle et al. 2018a; Demoule et al. 2018; Persichini et al. 2015). It has a good inter-rater and scale reliability. More recently, the Mechanical Ventilation–Respiratory Distress Observation Scale (MV-RDOS) has been designed to be more adapted to intubated patients (Decavèle et al. 2023; Decavèle et al. 2018b). **Figure 2** shows the main RDOS. An online calculator is available (https://dos-calc.pvsc.fr). Observation scales are an alternative way to identify dyspnoea when it cannot be self-reported.

Two electrophysiological indicators of dyspnoea are under evaluation in ICU patients. The first one is the electromyographic activity of the diaphragm (Decavèle et al. 2019) and extra-diaphragmatic inspiratory muscles (Schmidt et al. 2013). The second one is the electroencephalographic signatures of dyspnoea (Raux et al. 2019; Raux et al. 2007). These tools could help to detect and quantify dyspnoea regardless of the patient's level of cooperation. In the future, they could provide the opportunity for continuous monitoring of dyspnoea in intubated patients (Decavèle et al. 2023).

What is Clinically Important Dyspnoea?

Clinically important dyspnoea is defined as a dyspnoea-NRS ≥ 4, which corresponds to moderate intensity when compared to verbal descriptors (Wysham et al. 2015). By analogy with pain, a pain-NRS ≥ 4 is also the cut-off for moderate-to-severe pain and constitutes a clear indication for a prompt analgesic prescription (Devlin et al. 2018). Finally, dyspnoea-NRS ≥ 4 is associated with poorer outcomes (i.e. weaning failure, non-invasive ventilation failure and hospital mortality in patients receiving non-invasive ventilation (Bureau et al. 2022; Chen et al. 2017; Haugdahl et al. 2015; Dangers et al. 2018). However, in a study assessing whether a given level of dyspnoea is acceptable to patients, 30% of patients with ratings less than 4 considered their discomfort to be unacceptable (Stevens et al. 2019).

Regarding observational scales, an IC-RDOS score of 2.4 predicts a dyspnoea-VAS ≥ 4 with 72% sensitivity and 72% specificity (Persichini et al. 2015), and an MV-RDOS score of 2.6 in intubated patients predicted a dyspnoea-VAS>3 with

57% sensitivity and a 94% specificity (Decavèle et al. 2018b; Campbell et al. 2017).

Conclusion

Dyspnoea, an extremely distressing experience, is observed in approximately half of mechanically ventilated patients. When present, the intensity of dyspnoea is high. Dyspnoea has multiple deleterious consequences, including immediate suffering with a fear of dying and a strong association with anxiety. Dyspnoea also has long-term consequences, such as dark recollections of the ICU stay and a high prevalence of post-traumatic stress disorders. Like pain, dyspnoea is a self-reported symptom that imperfectly relates to physiological abnormalities. In mechanically ventilated patients able to communicate, the self-report of dyspnoea should be elicited as soon as possible during the ICU stay. In patients who are unable to communicate intentionally, it is possible to use an observational scale. When dyspnoea is present, the following interventions might be initiated to relieve it: reassurance of patients regarding their dyspnoea, reduction of non-respiratory stimuli of respiratory drive, minimisation of respiratory impedance and alterations of gas exchange, optimisation of ventilator settings, non-pharmacologic interventions such as air flux to face and relaxing music and, finally, a pharmacologic approach.

Conflict of Interest

Alexandre Demoule reports grants from the French Ministry of Health, Assistance Publique – Hôpitaux de Paris, Lungpacer, Respinor, consulting fees from Respinor, Lungpace, Lowenstein, Tribunal administrative de Cergy, Liberate Medical, payment or honoraria for lectures, presentations from Fisher & Paykel, Baxter, Getinge, Astra, Agence Européenne Informatique, Mindray, support for attending meetings and/or travel from Lungpacer, outside the submitted work. Maxens Decavèle reports support for attending meetings and/or travel from Isis medical outside the submitted work.

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The Hazards of Monitoring – Alarm Fatigue in the ICU

Alarm fatigue is a pressing clinical problem in our post-pandemic ICUs and can adversely impact patient outcomes. Its root causes can be classified by patient, device and organisation related. We believe it can be mitigated and we propose interventions through attention to policy, education and the creation of a meaningful culture of safety.

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"There are more things to alarm us than to harm us, and we suffer more often in apprehension than reality"

Seneca the Elder

Introduction

In 1983, there were an average of six different alarms in the ICU (Kerr and Hayes 1983). Fast forward 30 years, and this has exploded to over 40 potential monitors (Borowski et al. 2011). Continuous physiological monitoring of critically ill patients is now fundamental to healthcare provided in settings such as intensive care units, emergency departments, and operating rooms. Vital sign monitors are regarded as the sine qua non of advanced, safe, critical care. In short, they are critical to how we triage care and the numbers they display are afforded equal importance as the physical exam and laboratory findings. In addition to providing raw numbers such as heart rate, respiratory rate and blood pressure, continuous waveforms also provide surrogate measures of cardiac contractility and compliance, and biochemical health. In the event of significant variance from the "normal" physiology, these monitors will alert the bedside clinician, or others remotely, using auditory and visual alarms, and even text messages and emails. Electronic monitors have become our sentinels- in that they are on guard, minute by minute, for each of our patients- a level of vigilance that would be hard for any healthcare professional to maintain and to offer the potential to recognise early warning signs of acute deteriorations. Sometimes, the presence of such levels of monitoring has unfortunately and mistakenly been used to supplant patient reassessments through repeated physical exams and clinical acumen. Indeed, the word "monitor" itself comes from the Latin "to warn". But do they achieve this goal? Are they, and should they be heeded?

This seemingly constant desire to monitor more and more is not without consequences. For some patients in intensive care settings, the number of alarm signals may exceed nine hundred per day (Graham and Cvach 2010). Each time an alarm is activated, the bedside clinician is interrupted from their current task and required to 1) identify which patient is affected, 2) identify which device is alarming; 3) determine if it is critical, urgent or non-urgent; 4) establish if it is actionable or non-actionable; and 5) pinpoint the type of action required. This interruption causes lasting distraction and loss of focus. As more hospitals become completely digitised, the possibilities of new alarms reflecting better integration of deteriorating physiological and laboratory parameters as part of early warning systems (EWS) are only increasing. Artificial intelligence (AI) may refine such alarms and increase the frequency of only actionable alerts. However, such sophisticated engagement with AI will take time to develop and will present its own adverse consequences.

Estimates are that more than 85-95% of alarms in the intensive care unit are non-actionable, "false alarms" (Ruppel et al. 2018). We might alternatively use the term "false alarm" in such situations. In everyday life, this expression usually comes with a sense of relief and reassurance that there is no fire or burglar, and in hospital settings, there is no actual code blue. Of note, the frequency range of alarms from a patient's monitor in the ICU (2.5–3.15 kHz) is similar to a human scream or a baby's cry (Derbyshire et al. 2019). This is deliberate in its design. It grabs our attention by triggering a very human reaction of cognitive distress; a rapidly increased state of arousal, and a quick response time (Ruskin and Heuske-Kraus 2015). This barrage of non-actionable alarms and emotional escalation and de-escalation inevitably causes healthcare practitioners to develop defence mechanisms. We can become desensitised, mistrusting, and,

to a degree, apathetic towards the alerts. Together, this is called alarm fatigue, and it can have serious consequences on patient outcomes.

Despite many putative benefits associated with monitoring, more is not always more. While this article acknowledges the benefits of monitoring, our goal is to discuss alarm fatigue, its causes, and the challenges it poses in our post-pandemic ICUs, and to suggest ways in which its adverse effects can be mitigated moving forward.

Alarm Fatigue's Impact on Patients and Healthcare Providers

Over the last decade, there has been increasing interest in alarm fatigue as a risk to patient safety and occupational health. As such, it is a high-priority issue for healthcare organisations (Sendelbach and Funk 2013). This prioritisation of alarm management has been helped by the Joint Commission's (JCAHO) *National Patient Safety Goals (NPSG) on alarm management.* First issued in 2013 (Joint Commission, 2013), with its phase II released in 2016, the Joint Commission developed guidelines on alarm management after it issued a Sentinel Event Alert for 98 alarm-related incidents between January 2009 and June 2012. Of these events, 80 resulted in death, 13 in permanent loss of function, and five in unexpected additional care or extended stays. The Commission found that these sentinel events represent less than 10% of the actual alarm-related harms that occurred in hospitals.

Excessive alarms leading to alarm fatigue is associated with a prolonged length of hospital stay, increased morbidity and even increased mortality. The proposed mechanisms for this impact are the failure to respond to "true positive" alarms, due to desensitisation/deactivation of alarms, and decreased team performance, due to distraction and delays in patient care. For example, each interruption in a medication-related task is estimated to increase the probability of an error (after resumption) by 25% (Westbrook et al. 2010).

Following the COVID-19 pandemic, ICUs around the world have had to recruit large numbers of physicians, nurses, and inter-professional staff. Many of these new team members are starting their careers, in the ICU, rather than spending an initial period gaining experience in other hospital wards or ER first. This may lead to higher initial response rates to alarms. However, there is also a risk that these staff fail to recognise truly critical alarms. In other words, they are less likely to separate signals from noise. For new ICU team members, there is a natural and normal experiential gap that means you "are not as attuned to what is deserving of attention" and you "do not yet know what you do not yet know". Alarm fatigue is dangerous, especially when compounded by failure to escalate, professional insecurities, poor staff ratios, immature team culture, and unfamiliar team members and patient variables (Ede et al. 2019; Ede et al. 2021; O'Neil et al. 2021).

Aetiology of Alarm Fatigue

Many factors contribute to the clinical alarm burden and to the development of alarm fatigue in the intensive care unit **(Figure 1).**

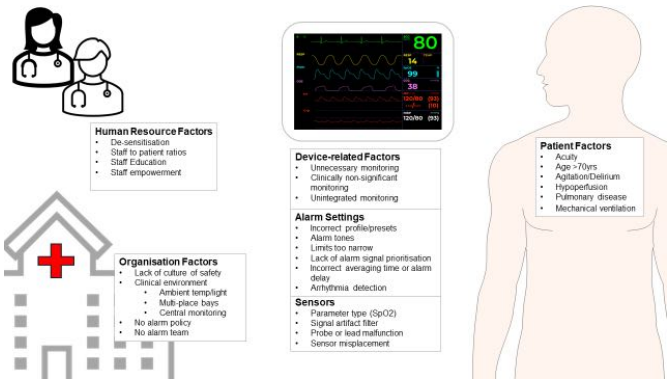

Figure 1. Causes of alarm fatigue

Patient-related factors

Amongst monitored patients in an ICU, two-thirds of alarms are generated by one quarter of the patients (Schondelmeyer et al. 2018), and as many as 77% of false alarms are generated by as few as 2% of the patients (Harris et al. 2017).

Perhaps the most important factor in the ICU alarm burden is patient acuity. Units with higher acuity will incorporate more medical devices and expect a higher degree of vigilance. Therefore, patients with cardiac and respiratory failure, and especially those requiring mechanical ventilation, have more false alarms and generate more alarm fatigue. Patients who are older than 70 years and confused and agitated will often move constantly. This becomes a significant cause of waveform disturbances, and this increases the frequency of cardiac rhythm and pulse oximetry alarms (Schondelmeyer et al. 2018).

Responding to the right alarms requires skill and judgement and, despite having both, we are still prone to suffer from anchoring biases. For example, we may assume alarms are solely due to a patient's confusion and agitation while failing to recognise the root cause of a patient's confusion and agitation. In other words, alarm fatigue can delay timely patient care. Furthermore, our previous responses to alarms, whether they were assessed to be actionable or not (rightly or wrongly), and whether appropriate support and action were provided by physician team members when needed are likely to impact our future responses. In other words, once we develop alarm fatigue and failure to recognise and rescue, it could become a self-perpetuating habit.

Device-related factors

Ideally, medical devices should have high diagnostic specificity and high positive predictive values (Cvach 2012). In other words, there should be few false positives or a few false "false" alarms. However, manufacturers of life-support systems, such as ventilators and monitoring systems, are under pressure to ensure that their products meet industry standards and they minimise legal liabilities with respect to any potential failure

to alert critical incidents. As such, alarms are highly sensitive and tend towards over rather than under alert. Consequently, they will have low specificity and low positive predictive value.

The sound that comes from medical devices should "speak" to the clinician and inform them of the issue, its priority and its severity; unfortunately, frequently, they do not. Intensive care physiological monitors usually present with four or more different alert tones based on the importance of the issue. These alarm level sequences escalate in importance, for example: "message", "advisory", "warning"," and critical". However, the "language" is specific to the manufacturer and device. Furthermore, devices at the bedside are rarely integrated and hence frequently "speak out of turn". Overlapping melodies reduce the listener's ability to discriminate (Lacherez et al. 2007). This can mean, for example, the ventilator is not automatically prioritised before the less important "nagging" feeding pump.

International safety standards must be met by medical devices, and this includes their alarm systems. The International Electrotechnical Commission first produced a standard for alarm systems in medical equipment in 2003. Its current iteration, IEC 60601-1-8, which was amended in 2012, is a comprehensive set of technical specifications for safety and performance requirements. It addresses the volume, pitch, duration, repetition, and priority of alarms in medical equipment. However, "standard requirement" is not synonymous with standardisation, nor is compliance with the IEC standard mandatory. Therefore, clinical staff transferring from one hospital ward to another or from one monitoring system to another often need to learn to "translate a new language" to safely care for their patients (Edgworthy et al. 2014).

We also need to consider that device sensors, electrodes, and cables. Improper sensor placement, or expired electrode pads, will increase impedance of the electrical signal, which can affect waveform measurement and analysis. Even simple interventions such as daily electrode changes, or the location of blood pressure cuff and the oxygen saturation sensor can affect alarm incidence by nearly half (47%).

The fundamental electrical component inside an invasive pressure monitoring system is the Wheatstone bridge in its transducer. Movement of the transducer will lead to "noise" interference of the waveform. This is often easy to identify. However, a corroded cable connection will dampen the electrical signal, causing lower amplitude waveforms, which underestimates the pressure. These errors all generate technical alarms which require a reaction (movement of sensor, or replacement of an electrode or cable). These are highly prevalent (Wilken et al. 2017).

Environmental factors

Excessive ambient noise in hospitals has been increasing steadily by 0.26dB annually (Busch-Vishniac et al. 2007). In ICU it can adversely affect patient outcomes, whether through sleep disruption, increased sedatives, and/or increased delirium. The World Health Organization (WHO) and the U.S. Environmental Protection Agency (EPA) have advocated that sound levels in hospitals be limited to 45 dB during the day and 35 dB at night. However, neonatal ICUs have average sound levels of 48–61 dB for up to 95% of the day, paediatric units average 53–73 dB,

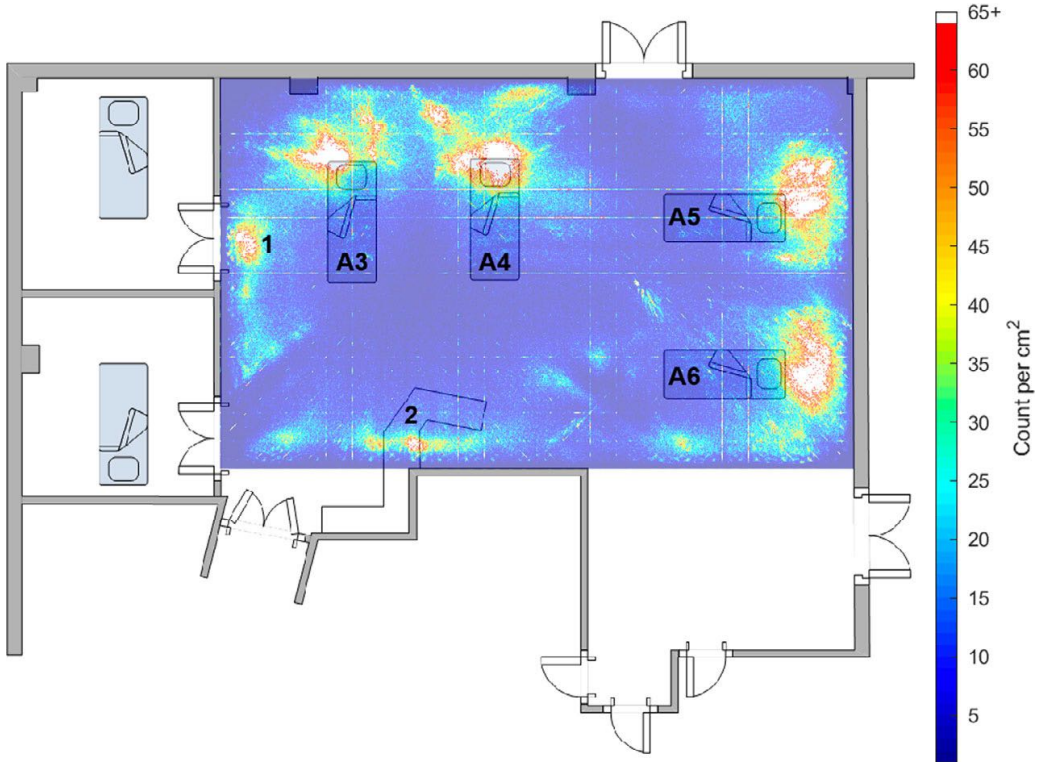

Figure 2. A heat map of noise in the ICU- From Derbyshire et al. 2019. Used with permission.
A heat map of the frequency and location from which noises above 35 dB originated from in an intensive care unit bay. The position of each of the four beds (A3-A6) in the bay is shown, as well as the work bench (1) and the desk (2). The grid lines are an artefact of the computational methods. (Source: Derbyshire et al. 2019).

What are expected warning signs of deterioration/what alarms may you see?	Have an open discussion when devising treatment plans with the ICU team on rounds. Discuss how EWS and their alarms may help with unanticipated deteriorations.
What alarms are worrying the ICU team members?	Do these alarms identify new changes? Did the frequency of alarms increase? Do they not understand what the alarms mean? Can they consult a more experienced colleague?
What can they do when alarms are sounding?	Recognise level of alarm (critical or not). Do they have means to test hypotheses they may have within scope of treatment plan and orders provided? And is the nature of the alarm one in which such hypothesis testing is reasonable action without calling for help? How long will it take to see a response or lack thereof?
What alarms do they need help with? What alarms do you need to ESCALATE?	These include critical alarms. Also includes consideration of integration with hospital escalation policies and protocols.
Who are you going to call?	Should always include the ICU team even though it may require interventions from other specialty teams, e.g. surgical, neurosurgical.

Table 1. Prevention of alarm fatigue: an approach engaging policy, education and ICU culture

and adult ICUs are 53–59 dB (Derbyshire et al. 2019). A significant proportion of this noise is from monitor alarms, typically located within 50cm of a patient's ears and producing default volumes greater than 50 dB. Moreover, as the important work by Derbyshire et al. (2019) has shown, the level of such noise can be experienced across the ICU setting (**Figure 2**).

The design of the ICU design has an independent impact on alarm fatigue. Clearly those cared for in multi-person rooms or bays will be exposed to greater ambient noise from other patient's monitors, devices of alarms. Any delays in pinpointing what alarm is sounding and from which patient may have critical consequences in such environments. Wherever possible, central monitoring stations, remote from the bedside, mitigate some of this noise pollution for patients, families and healthcare teams.

Organisation-related factors

Organisational policy also significantly influences the incidence and exposure to alarms in healthcare environments. Broadly speaking, the risk of alarm fatigue can be mitigated by a hospital's patient staffing models, training programmes and through the development of an institutional alarm policy.

The most important organisation-related factor for alarm fatigue is the empowerment of clinical staff to adjust alarm thresholds to their patient's clinical situation. Monitors usually have default setting profiles that are programmed by manufacturers. Many monitors also allow for defined profiles better suited to a patient's age, condition, or physiology. The probability of false alarms increases if the wrong profile is used, for example, adult defaults used for a paediatric patient or not adjusted to a patient's baseline values.

Organisations should develop formal clinical monitoring policies that clearly define the scope and circumstances where staff are safe and empowered to make changes and where this is dangerous and hence forbidden. Incorrect alarm limits affect their sensitivity, which can delay the recognition of a critical deterioration. This is particularly true when alarms are silenced because we assume the patient will remain stable. Any alarm policy should be tailored to the staff and promote their education and their understanding of medical devices and alarm management. As primary operators of monitoring systems, ICU nurses need adequate training and ongoing user support. However, research suggests that 60% of ICU nurses may have received insufficient monitoring training to properly manage alarms (Sowan et al. 2016). Initial training and ongoing support have been shown to improve alarm setting compliance and decrease the alarm burden (Brantley et al. 2016). Furthermore, any alarm policy should be linked to escalation of care policies to identify who should be called for help.

Where Do We Go From Here?

There are opportunities for change that can improve patient outcomes, and arguably, such change is needed now, following the recent pandemic, more than ever. These include developing and finessing hospital alarm policies and providing deliberate team-based education on both alarm systems and the causes and risks of alarm fatigue. Yet such measures may not be enough. Hospitals and ICU teams also need to create a culture of safety wherein if any team member is unsure of the significance of an alarm, they feel supported when they raise or escalate their concern and that dealing with alarms is a team responsibility, not just that of the bedside nurse or registered respiratory therapist. This culture shift can be encouraged by (**Table 1**):

1. All ICU team members being aware of what signs of deterioration may occur with any given patient and how EWS bolsters recognition of unanticipated deteriorations.

2. Encouraging team members to discuss any signs/alarms that worry them, even if they are uncertain or don't understand their significance.
3. Ensure all team members understand how to respond to alarms within their scope of practice. In other words, the freedom they have in accordance with treatment plans and/or existing orders and how long they have to establish if their hypothesis seems correct.
4. Ensure they can identify when they need help, i.e. when they need to escalate responses to alarms.
5. Ensure they understand who they need to call and when such calls must occur (e.g. when alarms are critical).

The equipment industry needs to meet IEC standards. Yet, such standards should also continuously evolve to meet patient and clinician needs. Industries have been concerned about alarm fatigue for some time and are already exploring the role of AI moving forward. It is time for us clinicians to be similarly engaged.

Conclusion

Alarm fatigue is a serious issue in the care of critically ill patients and is widely accepted as an independent factor that significantly and negatively impacts patient outcomes. It is of greater concern to us now, in this post-pandemic era, as we introduce, onboard, and train so many new team members. Alarm fatigue is multi-factorial and is affected by patient, device, environment, and organisational factors. Fortunately, many of these factors can be addressed within an ICU through policy change, education, and the promotion of a supportive culture of safety. There is hope for the future in mitigating alarm fatigue, but only if we tackle it as an inter-professional ICU team alongside our industry partners.

Conflict of Interest

None.

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Critical Care Monitoring: Time for Hospital-Wide Monitoring and Response Capabilities?

Physiological monitoring has a rich 200-year history. In this article, the authors look into the components of an ideal monitoring system and highlight how advancements in modern technology could enable the development of an effective continuous monitoring and response system.

The continuous monitoring of patient vital signs is a required standard in acute care and procedural settings. In these settings, monitoring provides data that are an integral part of diagnostic and treatment decision-making. As the cost and complexity of this technology come down, the question of dissemination to other areas inside and outside the hospital is inevitable. After all, isn't closer monitoring better? In this article, we will discuss the progress of continuous monitoring towards hospital-wide dissemination and why there is reason to hope that parallel advances in real-time analytics may allow us to overcome some of the traditional barriers to their widespread use as a valuable aid to clinical reasoning.

200 Years to Measure Blood Pressure – Monitoring Technology Takes Time to Refine

Heart rate, respiratory rate, and body temperature were three vital signs that could be measured without sophisticated instrumentation. During the first public demonstration of general anaesthesia by Dr Morton using ether in 1846 at Massachusetts General Hospital (MGH), Dr Heywood measured a patient's heart rate as an indicator of the depth of anaesthesia. Blood pressure was thought to be a better marker, but at the time, only invasive techniques for measurement were known. One hundred years previously, Reverend Stephen Hales measured a horse's blood pressure by inserting a glass tube into the carotid artery, an invasive method that was considered too risky for routine use in patients. It wasn't until 1855 when Von Vierordt of Tübingen introduced the first sphygmomanometer, that non-invasive blood pressure monitoring was possible. It took another 40 years for this technology to be refined (Riva-Rocci 1896) to the point where it was considered a sufficiently accurate method to measure systolic blood pressure and another ten years for Nikolai Korotkoff to establish a methodology to measure diastolic blood pressure with the aid of a stethoscope proximal to the Riva-Rocci cuff to identify the sounds associated with resumption of blood flow back into the previously occluded artery.

In the 1960s, Dr Maynard Ramsey III invented an automated oscillometric blood pressure monitor while he was a medical student at Duke University and created the company Applied Medical Research (AMR) to bring it to market. In 1976, AMR introduced the world's first microprocessor-based vital signs monitor, the "Device for Indirect Non-invasive Mean Arterial Pressure" (Dinamap 825). Thanks in part to the invention of intravascular catheters during the 1960s, continuous invasive arterial blood pressure monitoring became possible, and this remains the gold standard in continuous mean arterial blood pressure monitoring. From the 2000s to the present, there has been substantial investment in developing continuous non-invasive monitors of vital signs such as blood pressure. In general, these modern monitors rely on combinations of data elements such as heart rate (HR) and modified normalised pulse volume (mNPV), or pulse wave velocity (PWV), which involves a combination of an electrocardiogram (ECG) and a photoplethysmogram (PPG) to create their measurement. This approach has proven inaccurate and error-prone in non-ideal conditions, and at the time of writing, no FDA-certified medical-grade cuffless blood pressure monitors are available. This serves as a reminder of how difficult it can be to solve the engineering challenges associated with continuous physiologic monitoring.

Assuming engineers have done their job, and the device is accurately measuring physiologic data continuously and accurately, what's next? How do you integrate the device into the workflow of the clinical decision makers? How do you avoid overburdening them with data that is not helpful? The challenges of dissemination and implementation are considerable for a new device coming to market. Who puts the device on the patient?

Type of monitoring	On-demand	Continuous	Invasive	Non-invasive
Haemodynamic	BP (Blood Pressure) cuff	Swan-Ganz catheter	Swan-Ganz catheter	BP (Blood Pressure) cuff
Respiratory	Blood gas	Capnometry	Blood gas	Pulse oximetry
Neurological	Neurological assessment/scores	Electroencephalogram (EEG)	Intracranial pressure	Cerebral oximetry
Metabolic	Blood chemistry (labs)	Biosensors	Blood chemistry (labs)	Biosensors
Structural	X-ray based imaging	Ultrasound	Catheterisation	Electromagnetic based methods

Table 1. Patient monitoring modality examples

What happens if there is missing data? Who interprets the data? What actions are expected?

What would be the composition of an ideal monitoring system?

1. True representation of anatomical and physiological function of all human body organs and systems
2. Direct measurement or accurate indirect representation
3. Non-invasive rather than invasive with the ultimate goal of non-contact
4. Automated interpretation and presentation in a convenient package within the workflow of clinical decision-makers
5. Prediction of future changes
6. Real-time coupling with a response system that can evaluate the patient and initiate a diagnostic workup or treatment plan as needed.

New Sensors

Most current physiological sensors are based on established principles of physics, chemistry and materials science. Developing a new generation of non-invasive, continuous sensors requires breakthroughs in basic science as well as innovation in our approach to data integration. Examples of these sensors include electrochemical stickers (Wang et al. 2022), field-effect transistor (FET) sensors (Panahi and Ghafar-Zadeh 2023), interstitial fluid (ISF) sensors (Wu et al. 2024), magneto-inductive sensors (Zhu et al. 2024), graphene-based sensors (Huang et al. 2019), and other modalities that are currently in active development. The practical implementation of such sensors can have a profound impact on our ability to monitor physiological parameters non-invasively and continuously.

Rise of Artificial Intelligence

Recent advances in machine learning and artificial intelligence (AI) create opportunities to move closer to an ideal monitoring system. Recall that it was a combination of two technologies and observable data elements that led to the breakthrough in non-invasive blood pressure monitoring. How can AI help us progress towards the ideal physiological monitoring solution?

- **Dealing with indirect measurements.** Many currently available or promising technologies do not directly measure parameters of interest. Machine learning can correlate these measurements with a gold standard and use them in production systems.
- **Dealing with data resolution and missing data.** Novel techniques can use less data in established models.
- **Enabling predictive ability of monitoring system.** This is a well-known and advertised ability of ML/AI. To create such a system with accuracy (95+%), multimodal data and a complex system should be created. Future biological modalities, like genetic, cell-level data, etc., could potentially be used.
- **Automatic interpretation and ambient data representation.** This area is advancing particularly rapidly today. AI can interpret complex or data-dense sensor outputs, such as the automatic interpretation of electrocardiogram (ECG) waveforms. AI can also handle massive amounts of data and package it in a convenient way.

Development of Integrative Monitoring Modality With Actionable Prediction

With the current state of sensor technologies, data availability, and ML methods, we have as many opportunities as limitations to advance patient monitoring to the next level. One such modality would be the prediction of patient deterioration and alerting for potential actionable problems that could prevent the escalation of care. The current gold standard in hospitals is the Rapid Response Team (RRT), which has well-established criteria for activation. There is evidence that vital signs could predict RRT activation within twelve hours of emergency department admission (Walston et al. 2016). Still, the development and production of an integrated real-time system has its own challenges:

- Routine collection of vital signs on the hospital floor and in locations outside of the ICU (Intensive Care Unit)
- High throughput computer network abilities allow for the screening of hundreds and thousands of patients in real-time.

High accuracy of prediction models enables acceptance by clinicians without increasing cognitive load.

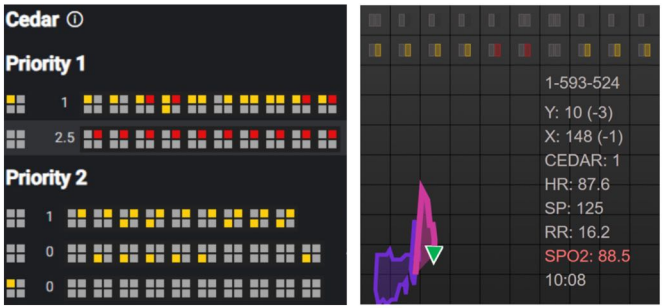

Figure1. The CEDAR (Clinical Events Detection and Response) visualisation will allow a clinician to quickly view an entire cohort of patient's health status and their suggested review priority in real time.

The Path to Effective Continuous Monitoring and Response Systems

To be effective, continuous monitoring must be linked to an appropriate response system. It is the combination of awareness and response that yields health outcome benefits. It is important to acknowledge that the path to effective continuous monitoring has to address some significant potential failure points:

- Quality of device data (missing data, more noise than signal)
- Variable connectivity of devices (companies advance their own ecosystem)
- Quality of alerts (too sensitive, not specific)
- Variability in effector arm response (vague expectations, inadequate training, staffing)
- Resistance to change (stakeholders not engaged, lack of understanding)
- Poorly executed implementation (missing readiness to implement measures)
- Missing evaluation steps
- Lack of trust

Failure of any of these components will cause the entire enterprise to perform poorly. Indeed, the Society of Critical Care Medicine just published a white paper on "Recognizing and Responding to Clinical Deterioration Outside the ICU," in which they make "no recommendation regarding the use of continuous vital sign monitoring" for this purpose in non-ICU patients (Honarmand et al. 2024).

We are exploring one approach to solving some of these challenges in our own institution. With access to the longitudinal patient record, real-time streaming of continuous device data, and advanced analytics, we are developing the Clinical Emergent Events Detection and Response CEDAR (Clinical Events Detection and Response) system for detecting and responding to patients outside of the ICU setting with indicators of clinical deterioration. By combining electronic health record data with device data and a targeted clinical review, we intend to monitor hospitalised patients with the intention of assigning a priority for targeted clinical review.

Conclusion

We are at a point in the 200-year history of monitoring technology where we expect to see new sensing modalities and signal processing techniques combined with other data sources in an integrated detection and response system that brings us closer to the ideal paradigm of continuous non-invasive predictive human monitoring. Our hope is that it will be much faster these days.

Conflict of Interest

None.

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Intravenous Landiolol for Rate Control in Supraventricular Tachyarrhythmias in Patients with Left Ventricular Dysfunction: A Systematic Review and Meta-Analysis

A systematic review investigating landiolol's efficacy in non-septic or post-operated SVT patients with concomitant left ventricular dysfunction.

Managing Supraventricular Tachyarrhythmias in Heart Failure: Landiolol's Role

The coexistence of heart failure (HF) and supraventricular tachyarrhythmias (SVT) exacerbates the clinical manifestation of one another, leading to worsened cardiac function and deteriorated haemodynamic status. Atrial fibrillation (AF), the predominant SVT in HF patients, contributes to tachycardia-induced cardiomyopathy, while HF results in atrial dilatation and fibrosis. This synergy increases the risk of cardiovascular death or hospitalisation compared to HF patients maintaining sinus rhythm (Mogensen et al. 2017).

In haemodynamically unstable AF cases, rhythm control is the preferred strategy, while rate control can be considered as the initial approach in stable patients. Beta-blockers are endorsed by European Society of Cardiology guidelines for rate control in heart failure with reduced ejection fraction (HFrEF) and mildly reduced ejection fraction (HFmEF). Digoxin may be used supplementary to beta-blockers in cases of persistent high ventricular rate or in the presence of contraindication to beta-blockers. Adequate rate control is a resting heart rate of ≤110 bpm, while lower targets (<80 bpm) and sinus rhythm restoration can also be aimed for if necessary (McDonagh et al. 2021).

Landiolol, an ultra-short-acting beta-1 blocker with the highest cardio selectivity (β1/β2 selectivity ≈ 255), offers rapid and precise heart rate reduction without significant blood pressure fluctuations. Its swift onset and offset make it suitable for acute management in critical conditions, including post-operative care, intensive care, and acute decompensated HF, showing promising outcomes. This systematic review investigated landiolol's efficacy in non-septic or post-operated SVT patients with concomitant left ventricular dysfunction.

Materials and Methods

The study, registered in PROSPERO (ID: CRD42023448712), adheres to the PRISMA guidelines. A systematic search of PubMed, Cochrane, Web of Science, and Scopus databases was conducted until July 14, 2023, using solely the term "landiolol". Additionally, the reference lists of all included studies were manually searched for further relevant articles.

Inclusion criteria covered adult SVT patients with left ventricular dysfunction, excluding septic or peri-operative cases. Exclusion criteria comprised case reports, paediatric studies, and non-English publications. Two independent investigators reviewed titles, abstracts, and full texts of potentially relevant papers, resolving discrepancies through consensus or consultation with a third author.

Data extraction involved gathering study details, population characteristics, follow-up duration, outcomes, and confounding factors. The primary outcome was targeted heart rate achievement (≥20% reduction from the initial heart rate AND final heart rate <110 bpm), while secondary outcomes included sinus rhythm restoration and adverse events or symptoms leading to drug discontinuation. Other parameters included were comorbidities (diabetes mellitus, hypertension, valvular heart disease, coronary artery disease), NYHA classification, prior medication, percentage reductions in heart rate and blood pressure, demographics, and pre-and post-treatment values of relevant cardiac parameters.

Quality assessment utilised the Newcastle-Ottawa Scale for cohort studies and the Cochrane Risk of Bias tool for randomised controlled trials.

Statistical analysis pooled data on target heart rate achievement, sinus rhythm restoration, and adverse events for landiolol-treated and non-landiolol-treated groups. Dichotomous outcomes were analysed via random effects meta-analysis to generate pooled odds ratios with 95% confidence intervals. Continuous outcomes were analysed similarly to pool mean differences. Heterogeneity was assessed using I2 statistic. Meta-regression wasn't possible due to limited studies. Publication bias was visually assessed with funnel plots. Analysis was conducted using Review Manager, Version 5.4., 2020, with significance set at $p < 0.05$.

Results: Efficacy and Safety of Landiolol

Out of 2304 initially retrieved articles, 15 studies met the eligibility criteria for the systematic review, with 11 included in the meta-analysis. Four studies compared landiolol to other antiarrhythmic

drugs (Nagai et al. 2013; Shinohara et al. 2020; Kimura et al. 2016; Kiuchi et al. 2017), while seven studies were single-arm (Adachi et al. 2014; Wada et al. 2016; Matsui et al. 2019; Oka et al. 2019; Kijima et al. 2017; Sakai et al. 2019; Iwahashi et al. 2019). Quality assessment of the aforementioned studies indicated a low risk of bias. A total of 1674 patients were included.

Landiolol's therapeutic impact was evident in its ability to significantly reduce heart rate, with a mean decrease of 42 bpm, a statistically significant finding ($p < 0.01$). Additionally, 75% of patients achieved the targeted heart rate, reflecting the robust effectiveness of landiolol in heart rate control. In comparison to alternative therapies, landiolol exhibited a pronounced superiority, with a pooled odds ratio of 5.37 ($p < 0.01$), underscoring its efficacy in heart rate management.

No discernible difference in sinus rhythm restoration was observed between landiolol-treated and non-landiolol-treated cohorts. Adverse events were reported in 14.7% of landiolol-administered patients, primarily attributed to dose-dependent blood pressure reduction. Notably, only a minor proportion (6%) necessitated landiolol discontinuation, with no supplemental interventions required to counteract blood pressure effects.

The rates of adverse events and drug discontinuation did not significantly differ between landiolol and other antiarrhythmic therapies, indicating a comparable safety profile. This favourable safety profile further enhances the appeal of landiolol as a therapeutic option for supraventricular tachyarrhythmias.

"landiolol's efficacy in managing tachyarrhythmias extends to diverse clinical scenarios, including acute decompensated heart failure, ventricular arrhythmias, septic and ICU patients"

Conclusion

In this meta-analysis, landiolol treatment resulted in significant heart rate reduction and achieved targeted heart rate in 75% of SVT patients with concurrent left ventricular dysfunction. In comparison with other antiarrhythmic medications (digoxin and diltiazem), landiolol showed superior effectiveness in targeted heart rate achievement, while there was no difference in sinus rhythm restoration. Landiolol demonstrated good tolerability, with only 6% of patients requiring drug discontinuation, mainly due to hypotension. Landiolol's efficacy in managing tachyarrhythmias extends to diverse clinical scenarios, including acute decompensated heart failure, ventricular arrhythmias, septic and ICU patients. While further randomised controlled trials (RCTs) are needed to establish its superiority in sinus rhythm conversion over other antiarrhythmic drugs, landiolol presents a superior option for heart rate management in heart failure patients, with favourable safety profile. These findings support its use as a viable treatment option in clinical practice, particularly in cases where other antiarrhythmic therapies may be contraindicated or poorly tolerated.

Disclaimer

This point-of-view article is sponsored by AOP Health and is part of the ICU Management & Practice Corporate Engagement or Educational Community Programme.

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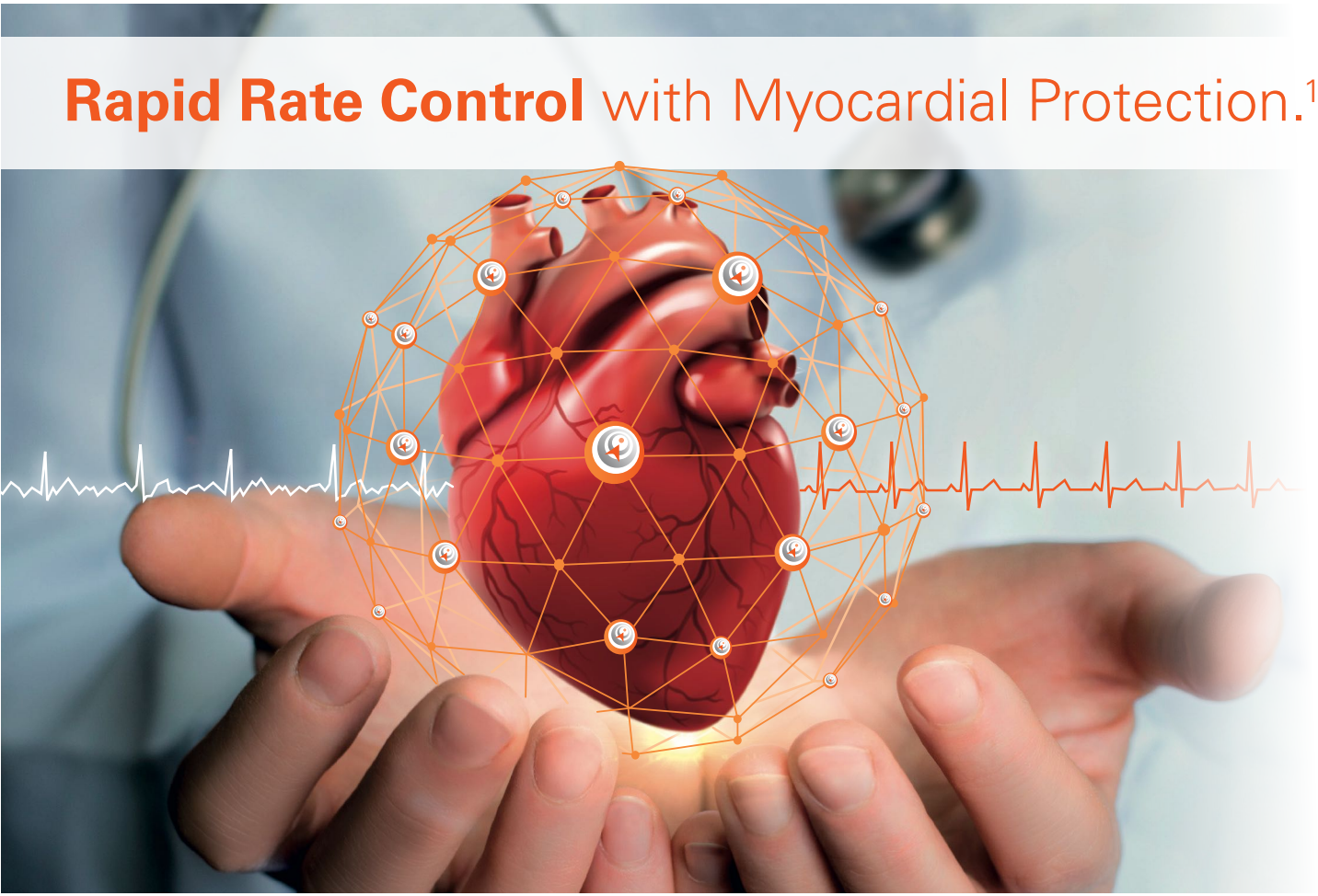
Landiolol hydrochloride

Rapid Rate Control with Myocardial Protection.[1]



Rapid control of ventricular rate in patients with SVTs and AF[1]

First-line for patients with cardiac dysfunction[2]

- **Limited effect** on blood pressure and inotropy[3]
- **Favourable safety profile for patients with renal and hepatic comorbidities** due to inactive metabolites and hydrolysis by plasma esterases[1,4]
- **Compatible with pulmonary disorder patients** due to highest cardioselectivity (β1/β2-selectivity = 255:1) among β1-blockers[5]
- **Limited rebound and tolerance effect** due to lack of pharmacochaperoning activity[6]

Rapibloc® 300 mg: Rapibloc® 300 mg powder for solution for infusion. **Composition:** A vial of 50 mL contains 300 mg landiolol hydrochloride which is equivalent to 280 mg landiolol. After reconstitution each mL contains 6 mg landiolol hydrochloride (6 mg/mL). Excipients with known effect: Mannitol E421, sodium hydroxide (for pH adjustment). **Therapeutic Indication:** Landiolol hydrochloride is indicated for supraventricular tachycardia and for the rapid control of ventricular rate in patients with atrial fibrillation or atrial flutter in perioperative, postoperative, or other circumstances where short-term control of the ventricular rate with a short acting agent is desirable. Landiolol hydrochloride is also indicated for non-compensatory sinus tachycardia where, in the physician's judgment the rapid heart rate requires specific intervention. Landiolol is not intended for use in chronic settings. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients, severe bradycardia (less than 50 beats per minute), sick sinus syndrome, severe atrioventricular (AV) nodal conductance disorders (without pacemaker): 2nd or 3rd degree AV block, cardiogenic shock, severe hypotension, decompensated heart failure when considered not related to the arrhythmia, pulmonary hypertension, non-treated phaeochromocytoma, acute asthmatic attack, severe, uncorrectable metabolic acidosis. For further information on warnings and precautions for use, interaction with other medicinal products and other forms of interaction, fertility, pregnancy, lactation, effects on ability to drive and use machines, unsiderable effects, and habituation effects, please refer to the published SmPC **Prescription only/available only from pharmacy. Date of revision of the text:** 09/2021.
Marketing authorization holder: Amomed Pharma GmbH, Leopold-Ungar-Platz 2, 1190 Vienna, Austria

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Perioperative Cardiac Output Monitoring: From Yellow Catheters to Green Algorithms

We discuss the economic and environmental advantages of green pulse wave analysis (PWA) techniques and the integration of PWA algorithms into standard bedside monitors that will likely contribute to democratisation of perioperative cardiac output monitoring.

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Haemodynamic instability frequently manifests during the perioperative course of high-risk surgical patients. This instability arises primarily during surgery due to the influence of anaesthetic agents on sympathetic activity and vascular tone, compounded by surgical bleeding. Post-surgery, various factors may be responsible for haemodynamic instability, including haemorrhagic complications, cardio-respiratory adverse events (such as myocardial infarction and pulmonary embolism), and infectious complications (e.g. septic shock). Haemodynamic instability can precipitate tissue hypoperfusion and hypoxia and, if prolonged, may culminate in organ failure, ultimately leading to postoperative mortality.

In this context, rational haemodynamic management requires quantifying cardiac output (CO) and vascular tone to identify the underlying mechanisms of haemodynamic instability and select the right treatment (**Figure 1**).

The Evolution of Haemodynamic Monitoring Tools

In the 70s, the introduction of the (yellow) pulmonary artery catheter allowed clinicians to better characterise haemodynamic profiles than with heart rate and blood pressure only. Both hypovolaemic and vasodilatory states, common during general anaesthesia and surgery, became easy to identify. Indeed, hypovolaemia is characterised by a decrease in cardiac filling pressures and blood flow (stroke volume and CO), whereas vasodilation is characterised by a decrease in systemic vascular resistance.

In the 90s, the development of less invasive and quicker-to-set-up oesophageal Doppler techniques led to the progressive decline of pulmonary artery catheter use during major surgical procedures (Wiener et al. 2007), with a few notable exceptions that include cardiac surgery (monitoring and manipulating pulmonary artery pressures may be useful in patients with right ventricular failure) and liver transplantation. Several studies have reported patient outcome benefits when using the oesophageal Doppler technique to guide perioperative haemodynamic management (Gan et al. 2002).

At the beginning of the 21st century, perioperative haemodynamic monitoring was further simplified by the inception of the arterial pulse pressure variation (PPV). This variable predicts fluid responsiveness without the need to track CO changes during a preload-modifying manoeuvre (e.g. a fluid challenge or a passive leg-raising manoeuvre) (Michard 2005). Several studies have reported patient outcome benefits when using PPV to guide intraoperative haemodynamic management (Benes et al. 2014). However, PPV cannot be used in all circumstances. During surgery with general anaesthesia, the main limitations to the use of PPV are laparoscopic surgery (increased abdominal pressure), thoracic surgery (open chest), and cardiac arrhythmia (mainly atrial fibrillation). Of note, a tidal volume of 7-9 ml/kg, commonly used during surgery and deemed safe (Levin et al. 2015), is compatible with the use of PPV.

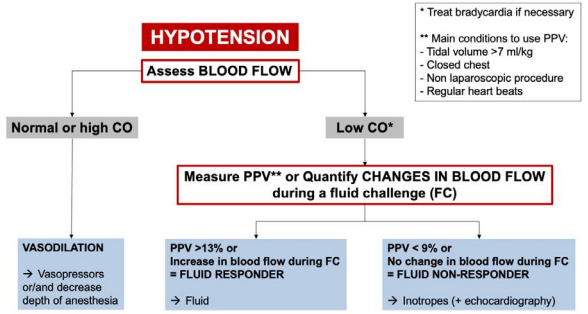

Figure 1. Rational haemodynamic management from blood pressure and blood flow monitoring. CO, cardiac output; PPV, pulse pressure variation.

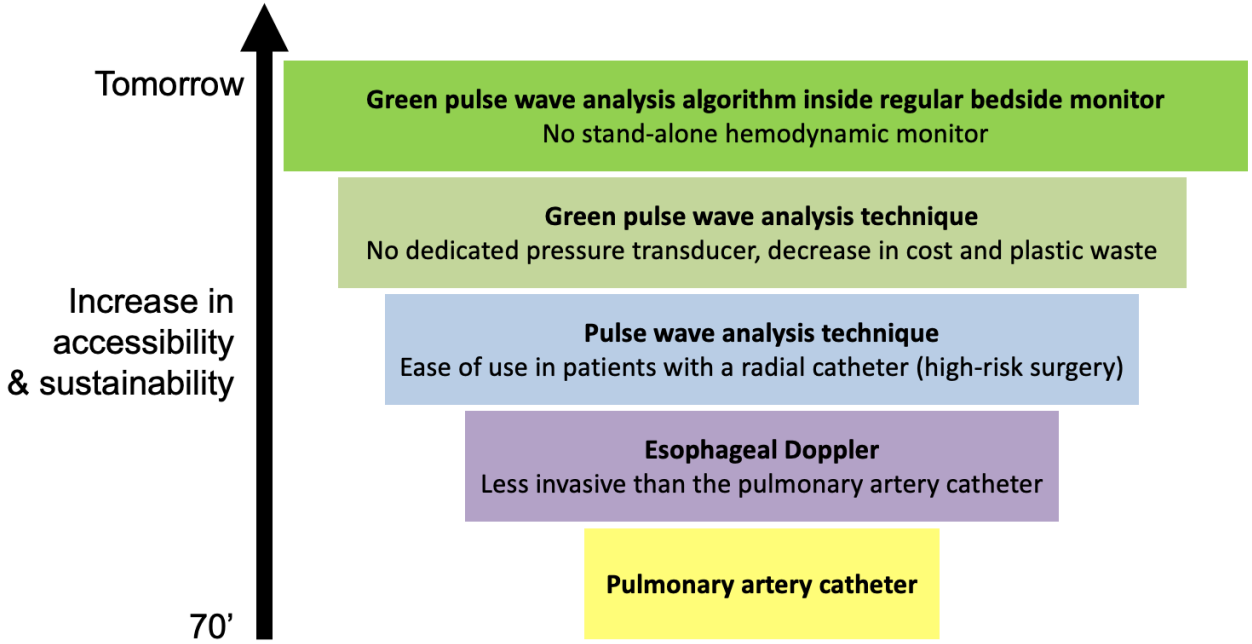

Figure 2. The evolution of perioperative cardiac output monitoring techniques, from the pulmonary artery catheter to integrating pulse wave analysis algorithms into regular multiparameter bedside monitors.

Pulse wave analysis (PWA) algorithms compute stroke volume and CO from the arterial pressure waveform (Chew et al. 2013). They allow clinicians to assess blood flow and vascular tone (total vascular resistance = mean arterial pressure divided by CO) in all patients who have a radial catheter in place for continuous blood pressure monitoring. Many studies have reported patient outcome benefits when using PWA techniques to guide perioperative haemodynamic management (Michard et al. 2017). The first PWA technique that did not require external calibration (with thermodilution or lithium dilution) was launched in 2005. Since then, multiple PWA techniques have become available. In a large European study done in 28 countries, 73% of anaesthesiologists who monitored CO during surgery did so with a PWA technique (Ahmad et al. 2015). This proportion increased to 92% in a recent European survey (Flick et al. 2023). Put differently, contemporary anaesthesiologists overwhelmingly favour PWA techniques as their primary method for monitoring CO (**Figure 2**).

How to Improve the Accessibility and Sustainability of PWA Techniques

Despite the development of PWA techniques, only 10 to 40% of surgical patients undergoing high-risk surgery have their CO monitored during the procedure (Molliex et al. 2019; Flick et al. 2023). According to a recent European survey, the main barrier to the clinical adoption of CO monitoring systems is their availability and cost (Flick et al. 2023). Addressing this financial challenge is pivotal to ensuring equitable access to advanced monitoring technologies and unlocking the full potential of PWA techniques. Recently, a nationwide French study (Michard et al. 2023) assessed the costs of using PWA techniques that work either with a dedicated pressure transducer or with any standard pressure transducer. Because of the significant cost difference between dedicated and standard pressure transducers (€150/transducer in the French participating centres), adopting standard pressure transducers for CO monitoring would reduce hospital costs by €67 million/yr. In France, this is the budget necessary to hire >2,000 nurses or to buy >10,000 pocket ultrasound devices each year. If, as recommended by the French Society of Anesthesiology and Intensive Care (SFAR), all high-risk surgical patients had their CO monitored (https://lnkd.in/esZkzZBe), the cost reduction would reach €187 million/yr. When extrapolating these findings to the European population and considering some specific pressure transducers may cost up to €300-400/unit, savings could exceed €1 billion/yr (**Figure 3**).

The climate crisis poses another significant challenge, prompting hospitals to actively seek solutions for reducing their carbon footprint. A growing trend is anticipated in the adoption of solutions that minimise plastic waste and mitigate carbon dioxide emissions (Davies et al. 2023). The above-mentioned nationwide French study (Michard et al. 2023) also compared the carbon footprint of PWA techniques requiring a dedicated pressure transducer to those working with any standard pressure transducer. Given the plastic weight difference between dedicated and standard pressure transducers, prioritising the use of standard transducers for CO monitoring would reduce plastic waste by 25 tons/yr and carbon dioxide emissions between 65 and 83 tons/yr. If the SFAR recommendations were followed, the reduction in carbon dioxide emissions would reach 179-227 tons/yr. When considering the additional packaging-related plastic waste (rigid plastic blister for dedicated pressure transducer vs soft plastic bag for standard pressure transducer) and extrapolating to the European population, the reduction would be close to 1000 tons of carbon dioxide (**Figure 3**). Thus, PWA techniques working with any standard pressure transducer, now known as "green" PWA techniques, are a preferable option both from an economic and environmental standpoint.

Whether green PWA techniques are as reliable as other PWA techniques is a legitimate question. Multiple studies have compared

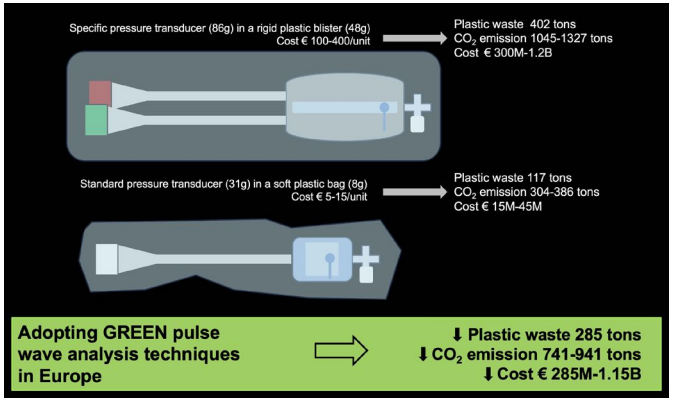

Figure 3. Yearly estimation of the environmental and economic impact of pulse wave analysis (PWA) techniques working with a specific pressure transducer or a standard transducer in Europe. The use of a standard transducer for cardiac output monitoring (green PWA techniques) would lead to a significant decrease in plastic waste and major savings. *Assumptions: European population = 450M, number of surgeries/yr = 20M, number of high-risk surgeries/yr = 3M.*

both green and other PWA techniques to reference CO measurements (by thermodilution or echocardiography) and have yielded conflicting results, depending on the patient population and the clinical situation. Only a limited number of clinical studies have compared several PWA techniques to a reference method in the same patients at the same time. Two studies (Hadian et al. 2010; Lamia et al. 2018) compared the LiDCOrapid and the FloTrac algorithms to reference pulmonary thermodilution in postoperative cardiac surgery patients. The lowest bias, the narrowest limits of agreement, and the best concordance rates to track changes in thermodilution CO were observed with the LiDCOrapid algorithm. Another study (Romagnoli et al. 2013) compared the MostCareUp and the FloTrac algorithms to reference echocardiography in patients undergoing vascular surgery. This study reported a better precision (i.e. a lower percentage error) with the MostCareUp algorithm. Interestingly, both the MostCareUp and LiDCOrapid are green PWA techniques. Thus, head-to-head comparison studies published so far support the notion that favouring the use of green monitoring solutions will not be to the detriment of accuracy and precision.

Conclusion and Perspectives

Perioperative haemodynamic monitoring tools have undergone remarkable transformations over the past five decades, progressing from yellow pulmonary catheters to contemporary green PWA techniques. In patients with a radial arterial catheter, PWA techniques have the advantage of instantly providing non-operator-dependent and continuous information about blood flow and vascular tone. Green PWA techniques not only reduce plastic waste but also contribute to significant cost savings in hospital expenditures, making them a recommendable solution.

Anticipating future developments, PWA algorithms are poised to integrate seamlessly into multiparameter bedside monitors, obviating the need for standalone haemodynamic monitors and further decreasing the cost and carbon footprint of haemodynamic monitoring. The forthcoming democratisation of CO monitoring holds the promise of empowering a growing number of clinicians to make timely and informed therapeutic decisions, ensuring a greater proportion of high-risk surgical patients benefit from advanced haemodynamic management.

Conflict of Interest

Frederic Michard is the founder and managing director of MiCo, a consulting and research firm based in Switzerland. Michelle Chew is the chair of the ESICM cardiovascular dynamics section. Pierre-Grégoire Guinot received fees for lectures from Baxter, Edwards, and Vygon.

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Technical Alarms During Continuous ECG Monitoring in the Intensive Care Unit

An analysis of technical alarms to guide hospital-based alarm management strategies and inform monitoring manufacturers on needed improvements to technical alarm algorithms used in bedside ECG monitors.

Introduction

Hospital-based electrocardiographic (ECG) monitors are configured to alarm for a number of different types of arrhythmias, ST-segment changes, and QT interval lengths that are designed to alert busy nurses. However, accurate detection of ECG abnormalities/features requires a clean signal. Most ECG devices include technical and/or inoperative alarm algorithms that are designed to notify and inform the nurse when a specific signal quality issue arises to minimise monitoring interruptions. For example, one type of technical alarm is ECG lead off (single or multiple), or ECG leads fail (no signal) that informs the nurse to replace either the skin-electrode(s) and/or the lead wire(s). Technical alarms can be configured to either generate an alarm sound (e.g., warning, continuous foghorn tone) or as an inaudible text message alert that flashes on the bedside monitoring screen. While there are no established guidelines for optimal alarm settings, technical alarms for artefact (noisy signal) or when a single ECG lead is off are typically configured as inaudible text message alerts (flash text on the bedside monitor); thus, they do not need to be silenced by the nurse. In general, inaudible text is selected for these types of alarms because there is still an ECG signal present; thus, arrhythmia detection is maintained. Many hospitals choose to configure some more important technical alarm types using an audible alarm configuration to ensure that a clean ECG signal is established promptly. For instance, when more than one ECG lead is off, or there is an extended period of time in a technical alarm condition (sustained artefact), an audible alarm is used since both of these types of technical issues may turn off or suspend arrhythmia detection software and an arrhythmia could be missed.

While technical alarms (i.e., artefact, ECG lead(s) fail, ECG lead(s) off) are designed to ensure optimal ECG signal quality for arrhythmia detection, these types of alarms are extremely common and can contribute to alarm fatigue in nurses. In a comprehensive one-month ECG alarm study in 461 intensive care unit (ICU) patients of the more than 2.5 million total alarms generated, 32% (791,632) were technical alarms (Drew et al. 2014). Alarm fatigue associated with bedside ECG and physiologic (vitals sign) monitors can create the following unsafe situations in patient care: (1) inadvertently ignoring alarms due to desensitisation (i.e., alarm noise is assimilated into a nurses' workflow); (2) lowering the volume of alarms to reduce patient and family stress from alarm noise; (3) completely silencing alarms; and/or (4) delayed response to alarms (Bonafide and et al. 2015). Additionally, nurses often experience overload in various forms during their work (e.g., cognitive and physical), which is further compounded by ECG device-related alarm fatigue (Lewandowska et al. 2020).

Alarm fatigue and the related responses set the stage for a major patient safety issue, which has devastating effects on both nurses and patients. Alarm fatigue has been associated with over 650 hospital deaths (Dee et al. 2022; Ruskin and Hueske-Kraus 2015), and in a retrospective study from 2011, there were 216 patient deaths linked to issues with alarm fatigue (Shue and Ortiz 2019). Importantly, these data are dated, and because few

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substantive interventions have been introduced to solve alarm fatigue, morbidity and mortality are likely much higher.

There have been several hospital-based studies that have evaluated technical alarms generated from ECG monitors (Albert et al. 2015; Cvach et al. 2013; Drew et al. 2014; Graham and Cvach 2010; Sendelbach et al. 2015; Shue and Ortiz 2019; Watanakeeree et al. 2021). One observational study conducted in adult ICU patients showed that 32% (791,632) of more than 2.5 million total alarms were technical alarms, and the vast majority (358,277) were for artefact followed by single ECG lead fail (90,547) (Drew et al. 2014). Technical alarms for arrhythmia suspend and ECG leads off (no signal) were not reported. In a subsequent secondary data analysis from this study, artefact, ECG leads off/fail, and arrhythmia suspend were reported in ICU patients with a left ventricular assist device (Watanakeeree et al. 2021). Artefact was the most common technical alarm (96%) followed by ECG leads fail (3.5%) and then arrhythmia suspend (0.5%). Of the remaining studies, technical alarms were examined at pre- and post-quality improvement (QI) project implementation (Cvach et al. 2013; Graham and Cvach 2010; Sendelbach et al. 2015; Shue and Ortiz 2019), and one examined alarm rates when using disposable versus non-disposable ECG lead wires (Albert et al. 2015). Two studies examined both artefact and ECG leads off/fail alarms (Albert et al. 2015; Sendelbach et al. 2015), two examined both ECG leads off and arrhythmia suspend (Cvach et al. 2013; Graham and Cvach 2010), and one examined only ECG leads off (Shue and Ortiz 2019). To our knowledge, no study has examined specific technical alarm types in a comprehensive manner (i.e., types, duration, possible patient/clinical factors). A more extensive analysis of technical alarms for these characteristics may help guide hospital-based alarm management strategies and inform monitoring manufacturers on needed improvements to technical alarm algorithms used in bedside ECG monitors.

Purpose

The purpose of this study was twofold: (1) examine the number, type, and duration of technical alarms for artefact; arrhythmia suspend, and ECG leads fail, and (2) examine whether demographic (age, sex, race) factors, clinical features (body mass index, impaired cognitive status, tremor, smoking), mechanical ventilation and/or ICU type (cardiac, medical/surgical, or neurological,) are associated with technical alarms.

Methods

Study Design

This was a secondary data analysis using data from a comprehensive one-month alarm study among a consecutive cohort of adult intensive care unit patients (Drew et al. 2014). The occurrence rate, type, and clinical features hypothesised to increase the occurrence of technical alarms (described below) for the artefact, arrhythmia suspend, and ECG leads fail were examined for this analysis. The Institutional Review Board (IRB) approved the study (IRB# 12-09723) with a waiver of patient consent because the alarm data was captured in the background, did not interrupt patient care, and was analysed retrospectively.

Sample and Setting

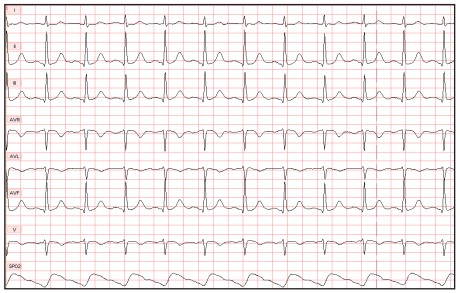
The primary study included 461 consecutive adult ICU patients with continuous ECG monitoring from three types of ICUs, including cardiac (16 beds), medical/surgical (32 beds), and neurological (29 beds), at a large tertiary-quaternary medical centre over a 31-day period. For this study, based on our prior work (Bawua et al. 2022; Drew et al. 2014; Harris et al. 2017; Suba et al. 2019), we hypothesised that BMI, being a current smoker, having cognitive impairment, a tremor, or mechanical ventilation would be associated with a higher rate of technical alarms. There were five patients (1.08%) who did not have BMI documented and were subsequently excluded, leaving 456 ICU patients available for analysis. Demographics, including sex, age, race, and ethnicity, were obtained from the electronic health record (EHR). Additionally, ICU type (cardiac, medical/surgical and neurological) and the use of mechanical ventilation were acquired from the EHR.

Alarm Data Capture System

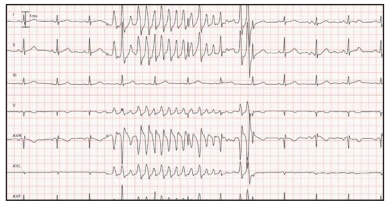
Our data capture system has been described in detail previously (Drew et al. 2014; Pelter et al. 2023). Briefly, all ECG and physiologic monitor waveforms (i.e., seven ECG channels [I, II, III, aVR, aVL, and aVF], arterial blood pressure, pulse oximetry [Sp02], impedance respirations), numeric vital signs, and alarm types (both audible and inaudible) were acquired via a secure data capture system. Data were downloaded to a secure research server approved by our hospital and were extracted into Extensible Markup Language (XML) files for analysis.

Technical Alarm Types

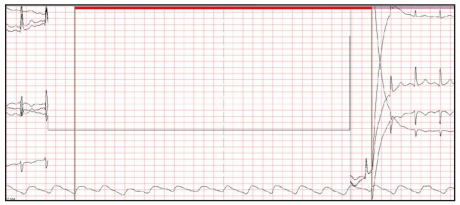
Technical alarm types, called system status alarms by the vendor, we examined included: (1) artefact (noisy signal); (2) arrhythmia suspend (no arrhythmia detection [software off] due to sustained artefact >20 seconds in the prior 30 seconds); and (3) ECG leads fail (no discernible ECG waveform displayed).



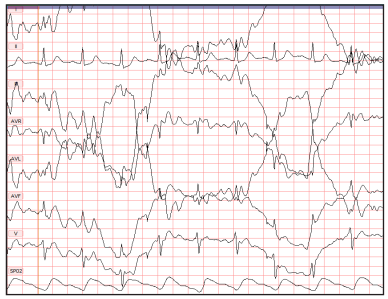
a) Clean ECG signal



b) Artefact



c) Arrhythmia suspend



d) ECG leads fail

Figure 1. Three types of technical alarms: a) clean ECG signal; b) artefact; c) arrhythmia suspend; and d) ECG leads fail. Shown on each ECG (top to bottom) are leads I, II, III, V (V1), aVR, aVL, aVF and Sp02 except B).

Figure 1 shows the type of technical alarms examined, as well as a clean signal ECG. Technical alarms greater than 20 minutes in duration were excluded as we assumed that this likely indicated that the patient was not being monitored (e.g., procedure on/off unit, bathing, etc.), but the monitor had not been paused. Alarms for artefact were configured in the bedside monitor as an inaudible text message alert. In this alarm condition, full arrhythmia processing is suspended while the lethal arrhythmia algorithm is still active. However, its accuracy may be hindered by the artefact. Alarms for arrhythmia suspend and ECG leads (plural) fail were configured as an audible warning alarm. In these alarm conditions, a repeating foghorn tone sounds, and arrhythmia analysis is suspended until the technical alarm condition is resolved.

Data Analysis

Descriptive statistics were used to describe sample demographics, factors hypothesised to increase the rate of technical alarms, ICU type, length of ICU stay (hours), and frequency and duration of each technical alarm. Descriptive statistics are reported as frequencies for categorical variables and mean Â± standard deviation (SD) for continuous variables. Data were tabulated in the overall sample and grouped based

Variable of Interest	n (%)
Demographics n=456	
Overall Age (mean ± SD, in years)	**60 ± 17**
Categories	
18 to 34	42 (9)
35 to 49	86 (19)
50 to 64	138 (30)
65 to 79	132 (29)
80 or older	58 (13)
Gender	
Female	208 (46)
Male	248 (54)
Ethnicity	
Hispanic	52 (11)
Non-Hispanic	396 (87)
Unable to state	8 (2)
Race	
Asian	74 (16)
Black or African American	35 (8)
Native Hawaiian or Pacific Islander	8 (2)
White	278 (61)
Unknown declined to state	61 (13)
Intensive Care Unit Type	
Cardiac (16 beds)	81 (18)
Medical Surgical (32 beds)	180 (40)
Neurological (29 beds)	195 (43)
Factors Hypothesised to Increase the Rate of Technical Alarms	
Body Mass Index (kg/m2)	28.1 + 8
Cognitive Impairment	195 (43)
Current Smoker	69 (15)
Mechanical Ventilation	179 (39)
Tremor	35 (8)
Intensive Care Unit Length of Stay (hours)	
Mean + SD	98.54 + 121
Median (IQR)	51 (26 – 113)
Number and Type of Technical Alarm	
Total of All Types	**572,763**
Artefact	557,018 (97.3)
Arrhythmia Suspend	3,378 (0.59)
ECG Leads Fail	12,367 (2.2)

Table 1. Demographics and clinical features of the 456 adult intensive care unit patients with technical alarms during continuous ECG monitoring.

Variable of Interest N=456 ICU Patients	Artefact 557,018 Alarms 451 Patients n (%)	Arrhythmia Suspend 3,378 Alarms 233 Patients n (%)	ECG Leads Fail 12,367 Alarms 438 Patients n (%)
Age (mean ± SD, in years)	60 ± 17	60 ± 18	59 ± 17
Sex (self-identified)			
Female	205 (46)	101 (43)	196 (45)
Male	246 (55)	132 (57)	242 (55)
Ethnicity			
Hispanic	52 (12)	27 (11)	51 (12)
Non-Hispanic	91 (86)	202 (86)	379 (86)
Unable to state	8 (2)	4 (2)	8 (2)
Race			
Asian	73 (16)	40 (17)	71 (16)
Black or African American	34 (8)	21 (9)	35 (8)
Native Hawaiian or Pacific Islander	8 (2)	5 (2)	8 (2)
White	275 (61)	138 (59)	264 (60)
Unable to state	61 (13)	29 (12)	60 (14)
ICU Type			
Cardiac (16 beds)	81 (18)	38 (16)	79 (18)
Medical Surgical (32 beds)	178 (39)	98 (42)	175 (40)
Neurological (29 beds)	192 (43)	97 (42)	184 (42)
Variables Hypothesised to Increase rate of Technical Alarms			
Body Mass Index (kg/m2)	28 + 8	28 + 8	28 + 8
Current Smoker	68 (15)	36 (16)	65 (15)
Cognitive Impairment	193 (43)	118 (51)	189 (43)
Tremor	35 (8)	27 (12)	35 (8)
Mechanical Ventilation	178 (40)	104 (45)	177 (40)
Monitoring Hours in ICU			
Mean + SD	99 + 121	144 + 149	102 + 123
Median	51	91	53
Minimum and Maximum	3 – 743	3 – 743	5 – 743
Number of Alarms			
Mean	1235 + 2568	15 + 31	28 + 59
Median (IQR)	363 (138 – 1,160)	4 (2 – 4)	9 (4 – 28)
Minimum - Maximum	1 – 21,752	1 – 256	0 – 795
Time in Alarm Condition During ICU Monitoring (minutes:seconds)			
Mean + SD	67:35 + 69	10:09 + 26	19:42 + 34
Median (IQR)	19:20 (6:42 – 60:39)	2:06 (0:34 – 9:03)	9:26 (3:09 – 22:56)

Table 2. Frequency of technical alarms in 456 ICU patients by type: artefact, arrhythmia suspend, and ECG leads fail compared by demographics, clinical features, ICU unit type and mechanical ventilation. Note: a patient could have more than one type of technical alarm.

Technical Alarm Type	Duration Category		
	2 sec to <5 min	5 min to <10 min	10 min to <15 min
Artefact 557,018 Alarms	552,561 (99.2)	3,343 (0.6)	1,114 (0.2)
Arrhythmia Suspend 3,378 Alarms	3,358 (99.4)	17 (0.5)	3 (0.1)
ECG Leads Fail 12,367 Alarms	12,293 (99.4)	50 (0.4)	24 (0.2)

Table 3. Technical alarms in 456 intensive care unit patients grouped by duration categories

on the type of technical alarm. For the statistical analysis, we used medians and interquartile ranges (IQRs) due to the high variability in the number of technical alarms a patient may have generated. For this analysis, IQRs were weighted (weighted median, weighted 25th percentile, weighted 75th percentile) by ICU monitoring time. A negative binomial GLM regression model was used to evaluate both univariate and multivariate associations because of the variability of alarm counts per patient. A p-value of <0.05 was used as the critical value to determine statistical significance. All statistical analyses were conducted using R (v4.3.2; R Core Team 2023).

As mentioned above, due to high variability in the number of all technical alarm types (i.e., one patient could have one while another patient could have hundreds), we used the following approach: (1) occurrence rates for each alarm type were calculated per 10 hours of monitoring; (2) median and 25th and 75th percentiles of the distribution were weighted by monitoring time, and; (3) a chi-square test was used to test for deviance of the binomial GLM, where a p-value of <0.05 was used to determine statistical significance. Predictors in the multivariate model were included based on subject-matter knowledge and the conceptual model. For this study, based on our prior work (Drew and Harris et al., 2014; Bawua and Miaskowski et al., 2022; Suba and Sandoval et al.,2019), we hypothesised that BMI, being a current smoker, having cognitive impairment, a tremor, or mechanical ventilation would be associated with a higher rate of technical alarms; hence, only patients with these variables documented were examined.

Results

Entire Sample

Table 1 shows the 456 adult ICU patients included in the study. The total number of technical alarms was 572,763. Of the total, 557,018 (97%) were artefact alarms, 3,378 (0.6%) were arrhythmia suspend alarms, and 12,367 (2.2%) were ECG leads fail.

Patient Characteristics by Alarm Type

Each technical alarm type was compared by patient demographics, ICU type, clinical features, and mechanical ventilation as illustrated in Table 2. All but 5 (n=451, 99%) patients generated one or more artefact alarms, 233 (51%) arrhythmia suspend alarms and 438 (96%) ECG leads fail alarms. It's important to note that a single patient could have more than one type of technical alarm. Patients in either the medical surgical or neurological ICUs had the highest proportion of alarms as compared to the cardiac ICU, which again likely reflects the number of beds in each unit.

The proportion of the three technical alarm types compared by, age, sex, ethnicity, race, ICU type, BMI, current smoker, cognitive impairment, tremor, and mechanical ventilation were equivalent (**Table 2**). Due to high variability in the number of technical alarms, the median values are discussed here and were used in the statistical analysis described below. Median ICU monitoring hours was longest in the patients with arrhythmia suspend alarms (91 hours), followed by ECG leads fail (53 hours), then artefact (51 hours). The highest median number of alarms was for artefact (363), followed by ECG lead fail (9), then arrhythmia suspend (4). The median time in an alarm condition was highest for artefact (19:20 min:sec), followed by ECG leads fail (9:26 min:sec), then arrhythmia suspend (2:06 min:sec).

Duration of Technical Alarms

Most of the technical alarms were two seconds in length, specifically, 58% (n=323,070) of the artefact alarms, 60.5% (n=2,044) of arrhythmia suspend alarms and 64% (n=7,915). Each type of technical alarm was categorised into duration time frames using the following categories, which could help guide alarm

Artefact Alarms Rates[1]				
Characteristics	**n=456**	**Median[2]**	**(IQR)[2]**	**p-value[3]**
Age, y.				0.08
18 to 34	42	94.7	(20.6 - 194.0)	
35 to 49	86	108.3	(39.6 - 169.9)	
50 to 64	138	99.8	(56.4 - 185.5)	
65 to 79	132	67.4	(23.2 - 135.2)	
80 plus	58	106.0	(28.2 - 148.3)	
Gender				0.60
Female	208	93.0	(40.0 - 165.0)	
Male	248	84.7	(36.9 - 175.7)	
Race				0.50
Asian	74	89.4	(26.2 - 164.9)	
Black or African American	35	67.2	(48.9 - 115.9)	
Native Hawaiian or Pacific Islander	8	77.8	(50.5 - 111.9)	
White	278	95.9	(35.0 - 196.7)	
Unknown or decline to state	61	86.2	(49.0 - 121.1)	
ICU Type				0.25
Neurological	195	86.2	(38.9 - 144.0)	
Medical-Surgical	180	99.3	(38.8 - 185.6)	
Cardiac	81	79.6	(23.3 - 173.1)	
BMI (kg/m2)				0.13
<25	183	88.7	(31.6 - 199.1)	
25-30	131	98.7	(37.4 - 160.9)	
30+	142	73.8	(42.7 - 134.6)	
Smoker				<0.001
No	387	77.8	(32.4 - 165.0)	
Yes	69	121.1	(78.0 - 180.7)	
Cognitive Impairment				0.41
No documented cognitive problem	261	83.9	(35.7 - 159.5)	
Cognitive problem documented	195	86.2	(37.1 - 185.6)	
Tremor				<0.001
No or undocumented	421	80.6	(35.4 - 150.9)	
Yes	35	197.5	(73.8 - 390.0)	
Mechanical Ventilation				0.01
No	277	112.8	(50.4 - 207.5)	
Yes	179	76.7	(30.9 - 137.1)	

Table 4. Occurrence rates of technical alarms for artefact by demographic, ICU type and factors hypothesised to increase the number of technical alarms in 456 ICU patients. [1]Rate is per 10 hours of monitoring. [2]Median and 25th and 75th percentiles of the distribution are weighted by monitoring time. [3]Chi-squared test for deviance of negative binomial GLM with single characteristic as predictor versus null model.

configuration delays and/or algorithm development: two seconds to <five minutes, five minutes to <10 minutes, and 10 minutes to <15 minutes. As shown in **Table 3**, 99% of all of the technical alarm types were in the two seconds to <five-minute category.

Univariate and Multivariate Analysis

Below we describe the univariate and multivariate analysis for each technical alarm type.

Artefact: In the univariate analysis, being a current smoker and having a tremor was associated with higher rates of artefact alarms. Being treated with mechanical ventilation was associated with fewer alarms (**Table 4). Figure 2** shows a forest plot of the multivariate analysis. Being a current smoker and having a tremor remained significant predictors of artefact alarms. Patients treated with mechanical ventilation were less likely to have artefact alarms. All of the other variables included were not significant.

Arrhythmia Suspend: In the univariate analysis, being a current smoker, having cognitive impairment and having a tremor was associated with higher rates of arrhythmia suspend alarms. Being treated with mechanical ventilation was associated with fewer alarms (**Table 5). Figure 2** shows a forest plot of the multivariate analysis. Being a current smoker, having cognitive impairment and having a tremor remained significant predictors of arrhythmia suspend alarms. Being treated with mechanical ventilation was associated with fewer alarms. All of the other variables included were not significant.

ECG Leads Fail: In the univariate analysis, age, race and having a tremor were associated with higher rates of ECG leads fail alarms. Being a current smoker, having cognitive impairment, and treatment with mechanical ventilation were not significant (**Table 6). Figure 2** shows a forest plot of the multivariate analysis. The race category of Native Hawaiian/Pacific Islander and unknown race (patient unable to state due to acute illness) were significant predictors of ECG lead fails alarms, but the sample was small. In addition, being treated in the cardiac ICU, having cognitive impairment, and having a tremor remained significant predictors of ECG leads fail alarms. Being treated with mechanical ventilation was associated with fewer alarms. All of the other variables included were not significant.

Discussion

To our knowledge, this is the first study to examine factors associated with three types of technical alarms, specifically artefact, arrhythmia suspend, and ECG leads fail, in 456 consecutive ICU patients. Artefact represented the vast majority of alarms, 97%, followed by ECG leads fail, 2.2%, then arrhythmia suspend, 0.5%. Fifty-eight percent of artefact alarms and more than 60% of arrhythmia suspend, and ECG leads fail alarms were two seconds in duration. Patients who were current smokers at admission were more likely to have artefact (1.16 times more likely) and arrhythmia suspend (1.98 times more likely) alarms. Having a tremor was associated with all three types of technical alarms (1.91 times more likely for artefact; 3.78 times more likely for arrhythmia suspend; and 1.84 times more likely for ECG leads fail). Documented cognitive impairment was associated with arrhythmia suspend (1.63 times more likely) and ECG leads fail alarms (1.30 times more likely). Being treated with mechanical ventilation was associated with fewer alarms for all three types of technical alarms.

Artefact

Of seven prior published studies that we identified as relevant to compare with our study, artefact was reported in four (Albert et al. 2015; Drew et al. 2014; Watanakeeree et al. 2021). Two were associated with this secondary data analysis and report the same findings as out study (e.g., the artefact was the most common type). Of the two remaining studies, one did not report specifically on artefact alarms but rather grouped artefacts with other types of alarms (Sendelbach et al. 2015). However, Albert et al. (2015) did report on artefact alarms. In their study, artefact alarm rates were examined by ECG lead wire type (disposable versus reusable) in 1,611 unique cardiac telemetry unit patients with 2,330 admissions. They found that artefact alarms were the second most common type of technical alarm (ECG leads off/fail most common), which is different than our study, where we

Arrhythmia Suspend Alarm Rates[1]				
Characteristics	**n=456**	**Median[2]**	**(IQR)[2]**	**p-value[3]**
Age, y.				0.10
18 to 34	42	0.3	(0.0 - 0.9)	
35 to 49	86	0.3	(0.0 - 0.8)	
50 to 64	138	0.4	(0.1 - 0.9)	
65 to 79	132	0.2	(0.0 - 0.4)	
80 plus	58	0.2	(0.0 - 0.4)	
Gender				0.07
Female	208	0.3	(0.0 - 0.6)	
Male	248	0.2	(0.0 - 0.8)	
Race				0.07
Asian	74	0.2	(0.0 - 0.4)	
Black or African American	35	0.2	(0.0 - 0.5)	
Native Hawaiian or Pacific Islander	8	0.1	(0.1 - 0.2)	
White	278	0.3	(0.0 - 0.9)	
Unknown or decline to state	61	0.3	(0.0 - 0.6)	
ICU Type				0.49
Neurological	195	0.2	(0.0 - 0.4)	
Medical-Surgical	180	0.3	(0.0 - 0.8)	
Cardiac	81	0.3	(0.0 - 1.0)	
BMI (kg/m2)				0.17
<25	183	0.2	(0.0 - 0.9)	
25-30	131	0.2	(0.0 - 0.8)	
30+	142	0.3	(0.0 - 0.6)	
Smoker				<0.001
No	387	0.2	(0.0 - 0.6)	
Yes	69	0.5	(0.1 - 0.9)	
Cognitive Impairment				0.007
No documented cognitive problem	261	0.1	(0.0 - 0.7)	
Cognitive problem documented	195	0.3	(0.1 - 0.8)	
Tremor				<0.001
No or undocumented	421	0.2	(0.0 - 0.6)	
Yes	35	1.0	(0.3 - 2.7)	
Mechanical Ventilation				0.009
No	277	0.3	(0.0 - 0.9)	
Yes	179	0.2	(0.0 - 0.6)	

Table 5. Occurrence rates of arrhythmia suspend alarms by demographic, ICU type and factors hypothesised to increase the number of technical alarms in 456 ICU patients. [1]Rate is per 10 hours of monitoring. [2]Median and 25th and 75th percentiles of the distribution are weighted by monitoring time. [3]Chi-squared test for deviance of negative binomial GLM with single characteristic as predictor versus null model.

ECG Leads Fail Alarm Rates[1]				
Characteristics	**n=456**	**Median[2]**	**(IQR)[2]**	**p-value[3]**
Age, y.				0.005
18 to 34	42	1.4	(1.0 - 2.9)	
35 to 49	86	1.8	(1.2 - 3.5)	
50 to 64	138	2.2	(1.3 - 3.2)	
65 to 79	132	1.6	(0.9 - 2.2)	
80 plus	58	1.7	(1.2 - 2.6)	
Gender				0.94
Female	208	1.7	(1.1 - 2.7)	
Male	248	1.7	(1.2 - 3.0)	
Race				<0.001
Asian	74	1.7	(1.0 - 2.1)	
Black or African American	35	1.2	(0.9 - 2.8)	
Native Hawaiian or Pacific Islander	8	1.6	(0.9 - 1.8)	
White	278	2.0	(1.3 - 3.4)	
Unknown or decline to state	61	1.6	(1.2 - 2.9)	
ICU Type				0.53
Neurological	195	1.7	(1.2 - 3.0)	
Medical-Surgical	180	1.7	(1.0 - 3.1)	
Cardiac	81	1.8	(1.3 - 2.7)	
BMI (kg/m2)				0.51
<25	183	1.6	(1.1 - 2.5)	
25-30	131	2.0	(1.1 - 3.3)	
30+	142	1.8	(1.2 - 3.3)	
Smoker				0.48
No	387	1.7	(1.1 - 2.8)	
Yes	69	2.2	(1.4 - 3.4)	
Cognitive Impairment				0.05
No documented cognitive problem	261	1.8	(1.2 - 2.7)	
Cognitive problem documented	195	1.7	(1.2 - 3.1)	
Tremor				<0.001
No or undocumented	421	1.7	(1.2 - 2.6)	
Yes	35	2.9	(1.5 - 5.6)	
Mechanical Ventilation				0.16
No	277	2.0	(1.2 - 3.1)	
Yes	179	1.7	(1.2 - 2.7)	

Table 6. Occurrence rates of electrocardiographic leads off by demographic, ICU type and factors hypothesised to increase the number of technical alarms in 456 ICU patients. [1]Rate is per 10 hours of monitoring.[2]Median and 25th and 75th percentiles of the distribution are weighted by monitoring time. [3]Chi-squared test for deviance of negative binomial GLM with single characteristic as predictor versus null model.

found the artefact was by far the most common alarm. Their study included cardiac telemetry unit patients, whereas ours included ICU patients. This may suggest that cardiac telemetry unit patients are more susceptible to leads off/fail, which is not entirely surprising given that these patients are more mobile than ICU patients who are mostly in bed. It is worth noting that in their study, the rate of artefact versus ECG leads off/fail was similar (2,993 artefact versus 3,555), suggesting that both types are common. Their study is interesting in that it showed that there were fewer artefact alarms in patients who had disposable ECG lead wires that were designed with a patented push-button feature. This study sheds light on one possible solution to reducing artefact alarms.

None of the studies examined patient-level factors associated with artefact alarms; hence, our study offers new information. We found that patients who were current smokers at admission or had tremors were more likely to have artefact alarms. Our study shows that patients with these characteristics may need more focused alarm management strategies and/or treatment(s). For example, the effects of nicotine withdrawal may need to be treated. Determining whether a tremor is part of the patient's history could be useful, or if new, it may suggest untoward effects of medications (i.e., drug induced Parkinson's) (Jeong et al. 2021; Shin and Chung 2012) Interestingly, being treated with mechanical ventilation was protective against artefact alarms. This is in contrast to prior studies our group has published showing that mechanical ventilation was associated with false arrhythmia and respiratory rate type alarms (Bawua et al. 2022; Harris et al. 2017). Sedation during mechanical ventilation may be one explanation, but this finding needs further investigation.

Arrhythmia Suspend

Of seven prior published studies that we identified as relevant to compare with our study, arrhythmia suspend was reported in three (Cvach et al. 2013; Graham and Cvach 2010; Watanakeeree et al. 2021). One was a secondary data analysis using our dataset that included only three patients with a left ventricular assist device. Arrhythmia suspend was the least common type, as was found in our study.

In a study by Cvach et al. (2013) arrhythmia suspend alarms were examined in a pre-and post-QI study assessing whether daily skin electrode changes reduced these types of alarms. The investigators showed that this type of alarm decreased by 60% in the medical progressive care unit and 74% in the cardiology care unit following the intervention. This suggests that daily skin electrode changes may reduce this type of alarm. However, patient and/or clinical characteristics associated with this type of alarm were not reported.

In a study by Graham et al. (2010), arrhythmia suspend alarms were examined pre- and post-QI implementation focused on several initiatives (i.e., changing default settings, education on individualising patient default settings, adjusting audible alarms, and a software modification) in the progressive care unit. Prior to the intervention, there were 634 arrhythmia suspend alarms, and after the intervention, they increased to 1,116. It is unclear why there were more of these types of alarms post-QI implementation, but overall alarm rates for a multitude of other alarm types were reduced post-QI implementation. One intervention used by the investigators was to adjust alarm settings (e.g., warning [foghorn tone] to an inaudible message) to reduce nuisance alarms (true but not actionable). However, it was not described whether arrhythmia suspend was adjusted in their study from a warning alarm to an inaudible message alert. If this adjustment was made, this might explain why there were more arrhythmia suspend alarms post-intervention. For example, if an alarm tone was not generated, the nurse would be less likely to solve this issue because it was set as an inaudible message alert. This type of technical alarm is generated when certain conditions are present, such as ECG leads off or, in the case of the monitor in place during this study, sustaining artefact>20 seconds in the prior 30 seconds. This indicates that arrhythmia analysis has been suspended (off), which has important clinical implications as an arrhythmia might be missed.

In our study, only 0.6% of the patients had this type of alarm, and the mean and median time a patient was in this alarm condition was 10 minutes and 2 minutes, respectively. We found that patients who were current smokers at admission and those

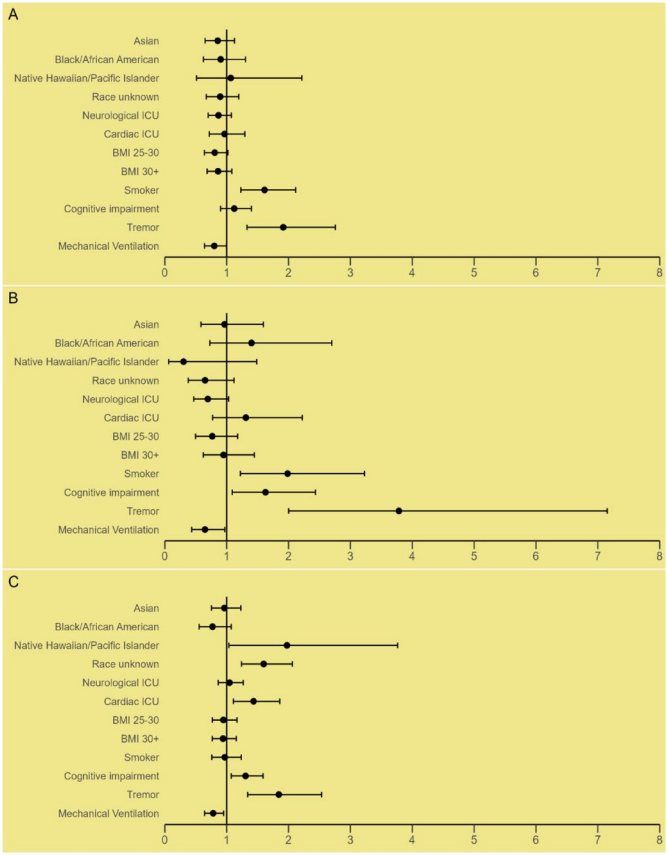


Figure 2. Forest plots of each technical alarm type: (a) artefact, (b) arrhythmia suspend, & (c) ECG leads fail.

with cognitive impairment or tremors were more likely to have this type of technical alarm. Therefore, nurses should assess for these patient characteristics and, if indicated, consult with the care team on strategies to minimise the effects of these clinical features (i.e., nicotine withdrawal treatment) if possible. These types of patients may also benefit from daily skin electrode changes, which have been shown to reduce artefacts that can create this type of alarm (Cvach et al. 2013; Sendelbach et al. 2015).

ECG Leads Fail

Contrary to artefact and arrhythmia suspend, all seven prior published studies that were relevant to compare to our study had measured ECG leads fail alarms (Albert et al. 2015; Cvach et al. 2013; Drew et al. 2014; Graham and Cvach 2010; Harris et al. 2017; Shue and Ortiz 2019; Watanakeeree et al. 2021). In the studies by Shue and Ortiz (2019) and Sendelbach et al. (2015), ECG leads fail alarms were measured, but grouped together with other types of technical alarms (e.g., no signal or telemetry battery low) or measured per day as a mean number of all ECG alarms. These two studies implemented several tests of change but it's not clear how these interventions specifically affected ECG leads fail alarm rates. Our study was designed to measure the occurrence rate of ECG leads fail alarms, which was found to be 2.2% (12,367) of all of the technical alarms. This type of data could be helpful in determining whether a reduction in ECG lead fail/off alarms are due to various interventions proposed in previous studies.

Two QI implementation projects had a specific focus on ECG leads fail/off alarms through several interventions, including daily electrode changing, custom alarm parameters, software modification, and clinician education (Cvach et al. 2013; Graham and Cvach 2010). Both studies by Cvach et al. (2013) and Graham et al. (2010) demonstrated an increase in the total number of ECG lead fail alarms by 39 and 314, respectively. In these instances, nurse susceptibility to alarm fatigue and exposure to audible alarms may have been reduced, but arrhythmia detection may also have been impacted. It's unclear whether this was a significant issue since the time in this alarm condition nor clinical features associated with this alarm condition were reported. Within our dataset, we found that documented cognitive impairment and tremors were associated with ECG lead failure. The mean time within this alarm condition was almost 20 minutes. However, the vast majority of lead fail alarms were between 2 seconds and 5 minutes. These findings offer important evidence that these types of alarms are generated after only a short duration of time in this alarm condition. One solution may be to add a delay for these types of alarms in the configuration setting. However, the optimal delay time needs further investigation to ensure patient safety.

In the study by Drew et al. (2014), 90,547 single lead fail alarms (inaudible messages) occurred over a one-month timeframe. It's important to note that ECG leads fail, which we report, will sound an audible foghorn tone. While their study only provided data for single ECG lead failure, our study showed that 99.4% of ECG lead failure alarms were between 2 seconds and 5 minutes in duration. Some of these are likely to be considered a nuisance and exacerbate the level of noise and possibly alarm fatigue within a busy ICU. In a secondary data analysis of this study in patients with an LVAD, there were 854 ECG lead fail alarms during a one-month time period (Watanakeeree et al. 2021). Even though this study provided valuable insight into a clinical feature that affected technical alarm rates in LVAD patients, generalisability is reduced since only three patients were examined.

ECG leads fail alarms can pose an increased risk for alarm fatigue and may compromise patient safety. A randomised study examining the difference in alarm events between disposable and reusable lead wires showed a decrease in the total number of all false alarms (i.e. no telemetry, leads off/fail artefact, and false crisis) when using disposable lead wires (Albert et al. 2015) Non-inferiority statistical analysis also demonstrated that disposable lead wires might be a reasonable approach as a potential solution for reducing technical alarms during continuous ECG monitoring.

Alarm Duration

For each type of technical alarm, the vast majority were found to be between two seconds and 5 minutes (99.2-99.4%). Duration of alarms between 5 minutes and 15 minutes was extremely uncommon (0.1-0.6%), which may suggest that current technical alarm algorithms are too sensitive and should be designed with a delay. As previously discussed, our evidence shows that clinical features (e.g., current smoker, documented tremor, or cognitive impairment, etc.) are associated with higher incidence rates for

certain types of technical alarms. Technical alarm thresholds should also be adjusted with the goal of reducing nuisance alarms caused by known clinical features from the patient's EHR.

Limitations

Several limitations warrant consideration. While we provide new information on the number and types of technical alarms, we did not correlate technical alarms with a patient's status at the time of the alarm (i.e., bathing, changing electrodes, repositioning, tests at the bedside, etc.). This means the nurse may have been at the bedside with the patient, and the alarm had minimal impact on alarm burden/fatigue. Because only one vendor's monitor was used, we do not know if our findings are generalisable to other device manufacturers. The study's retrospective design did not allow us to evaluate how alterations in alarm settings (e.g., turn off, adjust to inaudible setting) would impact the number of alarms identified. Despite these limitations, our study represents the most comprehensive evaluation of technical alarms in a consecutive sample of ICU patients done to date.

Conclusion

The vast majority of technical alarms were for artefact. Arrythmia suspend (software off) due to sustained artefact was uncommon. However, the mean time patients were in this technical alarm condition was 10 minutes, which could be important for ICU patients since arrhythmia detection may be compromised. Individual alarms lasted only seconds, which suggests that technical alarms are too sensitive and should be re-designed with a delay (e.g., 5 minutes) before alarming. Patients who were current smokers at admission were more likely to have artefact and arrhythmia suspend alarms. Having a tremor was associated with all three types of technical alarms. Documented cognitive impairment was associated with arrhythmia suspend and ECG leads fail alarms. Patients treated with mechanical vendtilation had fewer alarms (all three types). Patients with these features may require more guided alarm management strategies and/or treatment for nicotine withdrawal, or tremor as they are more likely to generate technical alarms.

Funding

This study was funded by the University of California, San Francisco (UCSF) School of Nursing Lipps Research Fund (Pelter, PI)

Conflict of Interest

None.

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Evidence of Ultrasonographic Monitoring in the ICU Patient

Ultrasound serves as a tool to enhance diagnostic precision for decision-making in life-threatening situations in the ICU. This article will delve into the evidence of ultrasound monitoring across different scenarios.

Introduction

In the contemporary landscape of medical diagnostics, ultrasonography stands out as a pivotal instrument, offering a non-invasive, cost-effective, and readily accessible modality for the real-time visualisation of internal anatomical structures. Its significance extends beyond mere imaging, serving as a critical adjunct in the decision-making process across various medical disciplines.

Ultrasonography's versatility is showcased through its application in diverse clinical scenarios, ranging from emergency medicine to chronic disease management. Moreover, ultrasonography's diagnostic precision is enhanced by the continuous advancements in ultrasound technology, including high-resolution imaging and Doppler capabilities.

Importantly, the real-time nature of ultrasonography permits a dynamic assessment of physiological functions, a feature unattainable by other imaging modalities.

Neurocritical Patient

Neuromonitoring is vital in the detailed management of individuals with traumatic brain injuries (TBI), enabling the swift detection of issues like increased intracranial pressure (ICP) (Martinez-Palacios et al. 2023). The diagnosis and treatment of ICP reduces morbidity and mortality (Chen et al. 2023).

The gold standard monitoring ICP necessitates the insertion of an invasive transducer into the parenchymal tissue or the brain ventricle, carrying potential risks of complications such as haemorrhage and infection (Raboel et al. 2012).

Ultrasound has become a preferred method for gauging the optic nerve sheath diameter (ONSD) owing to its convenience, functionality, safety, consistency, and lack of ionising radiation exposure or recognised adverse reactions (Montgomery et al. 2023).

The optic nerve is enveloped by a sheath derived from the meninges, stretching towards the orbit. This linkage allows for the movement of cerebrospinal fluid (CSF), thereby permitting analogous pressure shifts within the intracranial and orbital subarachnoid spaces. As a result, employing ultrasound to detect raised ICP via ONSD assessments is increasingly accepted in trauma, neurosurgical, and emergency medical settings (Fernando et al. 2019)

The fundamental procedures for measuring the ONSD via ocular ultrasound are outlined as follows:

1. Position the patient in a supine manner.
2. Apply gel to the closed upper eyelid, then place the high-frequency linear probe on it. This probe enhances the contrast between the nerve and the retrobulbar fat.
3. Manipulate the probe to visualise the entrance of the optic nerve into the globe.
4. The ONSD should ideally be measured 3mm posterior to the eye globe. The intersection point of the optic nerve and the ophthalmic artery is also a recommended site for measurement.
5. Obtain multiple readings for each eye and calculate the average to minimise the risk of variance (Richards et al. 2023).

Systematic review and meta-analysis showed a mean ONSD in the included studies of 5.82 mm (Monrtofano et al. 2021). ICP can be calculated using the formula ONSD = 5.69×ONSD –8.23 mmHg.

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To enhance the reliability of ONSD measurement, the introduction of the ONSD to eyeball transverse diameter (ETD) ratio was proposed (Vaiman et al. 2014). The transverse diameter of the eyeball and the sheath is measured and divided by this measurement; if it results in a value greater than 0.25, it indicates ICP (Du et al. 2019).

Transcranial Doppler (TCD) and transcranial colour-coded duplex sonography (TCCS) serve as essential real-time neurological monitoring instruments within the Intensive Care Unit (ICU). TCD ultrasonography can be conducted bedside to ascertain and monitor cerebral blood flow (CBF), gauged by mean blood-flow velocity (MFV), and ICP can be determined through Pulsatility Index (PI) values of the middle cerebral artery (MCA), as well as other major intracranial vessels, irrespective of the patient's level of consciousness or sedation status (Fatima et al. 2019). The PI stands out as a critical haemodynamic parameter offered by TCD/TCCS (Pinillos et al. 2021)

Patients with TBI who underwent diagnostic TCD monitoring for increased ICP or vasospasm (VSP) and exhibited abnormal TCD

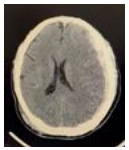
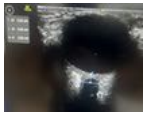
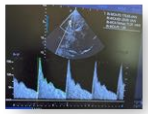
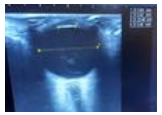
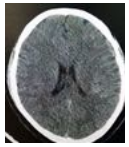
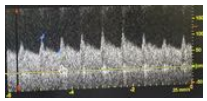
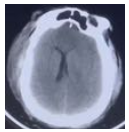
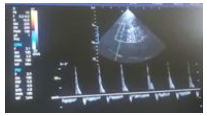
Clinical Presentation or Patient Symptoms	Suspected Diagnosis	Ultrasound Sign	Specificity	Sensitivity	AUROC	Decision or Management
Patient with anisocoria and low Glasgow Coma Scale 	Increased ICP	ONSD dilation 5.6-6.3 mm 	93%	96%	0.97	Invasive ICP measurement or management of intracranial hypertension
		Pulsatility Index >1.4 	85%	92%	0.85	
		ONSD/ETD Ratio >0.25 	82%	90%	0.92	
Patient with TBI isocoric pupils 	Rule out increased ICP	ONSD <5mm 	93%	96%	0.97	If sedated, proceed with sedation withdrawal. Initiate weaning protocol.
		Pulsatility Index <1.2 	85%	92%	0.85	
		ONSD/ETD Ratio <0.25	82%	90%	0.92	
Patient without brainstem reflexes and mydriatic pupils 	Brainstem death	**Cerebral circulatory arrest (CCA)** Flow patterns: oscillatory flow representing reversal of diastolic flow and systolic spikes representing lack of net forward flow. 	98%	90%	0.96	Brain death confirmed, withdrawal of life support, declaration of death, notification of family members. Notify organ procurement team.

Table 1. Ultrasound utilisation for clinical decision-making in neurocritical patient

findings (mean flow velocity [MFV] >120 cm/s or MFV <35 cm/s, PI >1.2) were more than three times as likely to experience a poor outcome compared to patients with TBI and normal TCD monitoring (Fatima 2019) The odds ratio (OR) for poor outcome in these cases was 3.87, with a 95% confidence interval (CI) ranging from 2.97 to 5.04, indicating a significant association (P < 0.00001)

It's important to note that despite its prognostic value, the use of TCD as a diagnostic tool for intracranial hypertension is not considered standard practice according to Robba and Taccone (2019) and not solely dependent on the PI > 1.4 because elevated pulse pressure, hypercapnia, hypocapnia, bradycardia, patient age, insonation angle, hypothermia, and hyperthermia can all influence the results of TCD examinations.

Brain Death

TCD is routinely employed as an ancillary test to confirm the absence of CBF. The identification of specific TCD patterns is crucial for determining cerebral circulatory arrest (CCA): these patterns include reverberating flow, systolic spikes, and the disappearance of previously recorded flow velocities (FV). The presence of the mentioned flow patterns across all major intracranial vessels is required to confirm brain death (Robba and Taccone 2019).

In a meta-analysis synthesis of 22 RCT, TCD was found a sensitivity of 90% and a specificity of 98%, when benchmarked against the gold standard (Chang et al. 2016).

Cardiac POCUS (FoCUS: Focused Cardiac Ultrasound)

One of the most sensitive (S) and specific € findings when scanning the heart is pericardial effusion (S:96%, E:98%), which, in the right context and with certain characteristics, becomes an absolute indication for immediate pericardiocentesis (Lau and See 2022).

The context would be a patient in a state of obstructive shock who, upon standard cardiac scanning (parasternal long and short axis, apical 4 chambers and/or subcostal), displays an anechoic image that separates the pericardial layers by at least 10 mm. If this distance is smaller, pericardiocentesis is contraindicated as it is considered a small effusion with little probability of being responsible for the state of shock, and with technical complexity for performing pericardiocentesis, the risk being greater than the potential benefit (Imazio and De Ferrari 2020). The echocardiographic signs we can find in cardiac tamponade are right atrial diastolic collapse (S: 95-100%, E: 70-80%), right ventricular diastolic collapse (S: 90-95%, E: 95-100%), respiratory cycle changes in the E wave velocity of the mitral flow > 25% and of the (Hamzaoui et al. 2013) E wave in the tricuspid flow > 40%, the last two signs are surrogates of the paradoxical pulse (S: 98%, E: 83%), dilation of the IVC (inferior vena cava) > 20 mm with a reduction in its variability (<50%) with the respiratory cycle (S: 95-100%, E: 40-50%).

Another immediate attention pathology is pulmonary thromboembolism (PTE), traditionally only diagnosed with pulmonary angiography or perfusion scintigraphy. However, since 2019, the European cardiology guidelines for PTE established echocardiographic signs that could aid in the diagnosis of high-risk PTE and make the decision for thrombolysis without waiting for angiography, as this study is not available in many hospital centres (Konstantinides et al. 2020). One of the most used signs of PTE is the growth of the right ventricle (RV) compared to the left ventricle (LV) with an RV/LV ratio > 1 (S: 50%, E: 93%). The D sign, referring to the abnormal flattening or bulging of the septal wall towards the LV due to RV pressure overload, has been reported with low sensitivity but high specificity for tamponade (S:29.7%, E: 96.2%). McConnell's sign, which includes akinesia of the RV-free wall with abnormal RV apical hyperkinesis due to anchoring with the LV fibres in a hyperdynamic state, has an estimated sensitivity of 29.1% and specificity of more than 98%. The combination of a reduction in TAPSE (tricuspid annular plane systolic excursion) <17 mm and the 60/60 sign (pulmonary valve acceleration time <60 ms and tricuspid regurgitation gradient <60 mmHg) have a sensitivity of 51% and specificity of 86% (Falster et al. 2022). Early systolic notching in the Doppler study of the pulmonary artery flow has been reported with a sensitivity of up to 97% and specificity of 99% with an area under the curve of 0.96 (Bigdelu et al. 2023).

Another indispensable evaluation in echocardiography is the determination of heart failure, as if established, it can have significant implications in the approach to a patient, generally to decide the initiation of inotropics or to halt fluid resuscitation.

E-point septal separation (EPSS) has a strong correlation with LVEF (left ventricular ejection fraction), traditionally the cut-off point to define that the LVEF is below 40% is >7 mm (McKaigney 2014); however, a cut-off of 9.5 mm has been recently proposed to establish an LVEF <40% with an S: 90%, E: 80% and an area under the curve of 0.91 (Núñez-Ramos et al. 2022).

MAPSE (Mitral annular plane systolic excursion) allows for the evaluation of longitudinal shortening of the LV; a measure of less than 8 mm is associated with an LVEF < 50% with an S 98% and E 82%, while a value of more than 10 mm (Schick et al. 2022) has an S 90% and E 87% for preserved systolic function (>55%).

In general, POCUS has high sensitivity and specificity in identifying the type of shock presented by patients. From 0.77 for distributive shock to 0.93 for hypovolaemic shock, with specificity ranges going from 0.92 for hypovolaemic to 0.97 for obstructive shock (Yoshida et al. 2023).

Lung Ultrasound

This can reduce imaging techniques involving radiation and decrease the taking of radiographs in critical areas by up to 50% (Brogi et al. 2017). The lung exploration can be done with any transducer on a simple ultrasound machine, dividing the thorax into 4 quadrants per lung and using both two-dimensional and M modes. Subsequently, it is necessary to describe the pleural line and the artefacts that originate from this line for the diagnosis of the different clinical scenarios (Demi et al. 2023).

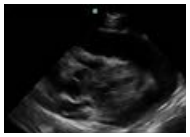
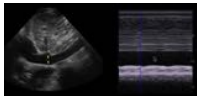
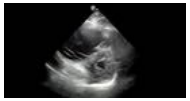
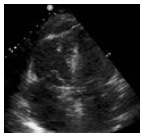
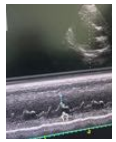
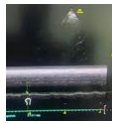
Clinical presentation	Diagnostic Suspicion	Echocardiographic Sign	Sensitivity	Specificity	Management Strategy
Signs of obstructive shock – Jugular vein distension. Muffled heart sounds. Hypotension unresponsive to vasopressors or fluid therapy. Comorbidity causing pericardial effusion. Electric alternans on EKG. Low voltage QRS complexes	Tamponade	Diastolic collapse of RA	95-100%	70-80%	Pericardiocentesis
		Diastolic collapse of RV 	90-95%	95-100%	
		Changes in E wave velocity in mitral flow >25%	98%	83%	
		IVC > 20 mm, variability < 50% 	95-100%	40-50%	
Signs of obstructive shock – Deep vein thrombosis. Risk factors for venous thrombosis. Tachycardia. Elevated D-dimer. S1Q3T3 on EKG.	PE (Pulmonary Embolism)	"D" sign 	29.70%	96.20%	Thrombolysis or Thrombectomy
		McConnell's sign 	29.10%	98%	
		Decreased TAPSE	51%	86%	
		60/60 sign			
		Systolic notch in pulmonary artery Doppler	97%	99%	
Heart failure Dyspnoea. Swelling of limbs or generalised. Jugular vein distension. Diffuse pulmonary crackles. Hepatojugular reflux.	Acute or Chronic Decompensated Heart Failure	EPSS > 9.5 mm 	90%	80%	Negative fluid balance, Inotropic support
		MAPSE < 8 mm 	98%	82%	

Table 2. Ultrasonographic Signs in Obstructive Shock and Heart Failure. RA: Right Atrium, **RV:** Right Ventricle, **IVC:** Inferior Vena Cava, **EKG:** Electrocardiogram, **EPSS:** E-point septal separation, M**APSE:** Mitral annular plane systolic excursion, **TAPSE:** Tricuspid annular plane systolic excursion

Acute Respiratory Failure

Lung ultrasound is sensitive to changes in lung aeration and density. Therefore, the increase in extravascular lung water, loss of aeration, or the combination of these phenomena modify the visualised image. In a meta-analysis with 1,232 patients, lung ultrasound had a sensitivity of 92 and a specificity of 98% for diagnosing the cause of acute respiratory failure. Pleural effusion and acute interstitial syndrome are the aetiologies most likely to be identified by lung ultrasound, reporting a pooled sensitivity of 95% (Yuan et al. 2021). Due to this diagnostic precision, international scientific societies issue strong recommendations for the use of lung ultrasound for the diagnosis of acute respiratory distress syndrome (ARDS), for the evaluation and classification of pulmonary oedema in heart failure, and for the evaluation of pleural diseases (Gargani et al. 2023).

Pneumothorax

Lung ultrasound presents 95% specificity for the diagnosis of pneumothorax when absence of pleural sliding and the barcode sign (also called stratosphere sign) are observed, and 100% specificity when the "lung point" sign is found respectively. The sensitivity is 90 to 95%, aiding in diagnosis when there is high clinical suspicion in patients with decreased mobility of a hemithorax, absence of respiratory sounds, hyperresonance on percussion, and some suspected cause (e.g., chest trauma, central venous access placement).

Pleural Effusion

In cases of pleural effusion syndrome, clinical presentation often includes observable signs such as decreased lung expansion on the affected side, diminished palpation and percussion, and reduced tactile fremitus. However, these clinical indicators exhibit low sensitivity and specificity. Utilising ultrasound as a diagnostic tool significantly enhances accuracy. Ultrasound findings typically reveal an intrapleural anechoic zone, commonly referred to as the sinusoid sign in M mode. The sensitivity and specificity of ultrasound in detecting pleural effusion range between an impressive 95% and 99%, respectively. This underscores the invaluable role of ultrasound in accurately diagnosing pleural effusion syndrome and guiding appropriate clinical manage-

ment. Moreover, ultrasound also enables clinicians to perform thoracentesis, facilitating the safe and precise extraction of pleural fluid for diagnostic and therapeutic purposes.

Consolidation

In the case of consolidation syndrome or pulmonary condensation, characterised by systemic inflammatory response data (fever, tachycardia) and respiratory failure (dyspnoea and low oxygen saturation) which are not very sensitive and specific, together with more sensitive clinical data such as productive cough with purulent expectoration, lung ultrasound complements these findings with a sensitivity reaching 89% and specificity up to 97% when finding an irregular or fragmented pleural line accompanied by subpleural hyperechoic echoes, known as the shred sign, in addition to dynamic air bronchograms observed as branching intraparenchymal hyperechoic images, making this tool superior to clinical diagnosis of this syndrome.

Interstitial Syndrome

The interstitial alveolar syndrome could hardly be differentiated clinically from another cause of acute respiratory failure if not for the findings on lung ultrasound, where we will find three or more vertical hyperechoic artefacts, which originate vertically from the pleural line in the form of comet tails, and erase the A-lines, it is necessary for these findings to be found in two different insonation zones, these artefacts are known as B-lines and have a sensitivity of 95% and specificity of 91% for the diagnosis of this syndrome.

Diaphragmatic Dysfunction Myotrauma Associated with Mechanical Ventilation.

Diaphragmatic Excursion: With a low-frequency transducer positioned longitudinally with the cephalic mark in the right subcostal region between the anterior axillary line and the midclavicular line, the posterior third of the right hemidiaphragm can be visualised in two-dimensional mode. During inspiration, there is a caudal displacement (excursion) that can be explored in M mode with the exploration line positioned perpendicular to the diaphragm. Absent or reduced excursion <10 mm during a spontaneous breathing trial indicates diaphragmatic dysfunction.

Diaphragmatic Thickening: With a high-frequency transducer perpendicular to the lateral thoracic wall in the mid-axillary intercostal region at the zone of apposition (between the 9th and 10th intercostal spaces), the diaphragm is identified 2 – 4 cm from the skin as a three-layer structure; an internal hypoechoic muscular layer surrounded by two hyperechoic external membranes (the peritoneum and the pleura). The thickness of the muscle at the end of expiration (at rest) and the thickening and stiffness of the diaphragm during inspiration should be analysed in two-dimensional or M mode. The lower limit for the normal thickness of the diaphragm in healthy individuals is 1.5 mm (Santana et al. 2023). Values lower than this can predict diaphragmatic atrophy. Also, a decrease of >10% in serial measurements of the diaphragm suggests atrophy (Goligher et al. 2015). The diaphragm thickening fraction is defined as the percentage change in the thickness of the diaphragm during inspiration. It represents the inspiratory effort of the diaphragm, and a value < 20% is useful for the diagnosis of diaphragmatic dysfunction (Inspiratory Diameter – Expiratory Diameter)/Expiratory Diameter)X100. In a recent meta-analysis, the diaphragmatic excursion has an S 80% and E 80%, and the thickening fraction an S 85% and E 75%; therefore, they have acceptable diagnostic accuracy as predictors of success for the withdrawal of mechanical ventilation (Parada-Gereda et al. 2023).

Focused Assessment With Sonography in Trauma: ECO-FAST

Trauma represents a significant cause of mortality in young individuals (Savoia et al. 2023). Closed abdominal injuries (solid organ injuries such as the liver or spleen, mesenteric and visceral tears) can cause significant bleeding and haemodynamic instability, with hypovolaemic shock being one of the main causes of trauma-related mortality (Stengel 2015).

According to the protocols established by Advanced Trauma Life Support (ATLS), the first step as a standard, quick, repeatable, economical, and reliable diagnostic tool for the early detection of intra-abdominal haemorrhage in patients with severe injuries is the performance of an abdominal ultrasound (Chaijareenont et al. 2020) or a focused assessment with sonography in trauma (FAST).

The FAST protocol is based on the principle that free fluid (FF) such as blood can accumulate in certain anatomical locations in the supine patient, its main objectives being to identify FF and at the same time guide decision-making in the resuscitation stage, mainly in the polytraumatised patient (Gallardo et al. 2023).

Whom, where, and when to apply the fast or e-fast protocol?

There are three important indications for performing the FAST protocol:

1. Closed abdominal trauma with haemodynamic instability.
2. Penetrating trauma in the thoracoabdominal transition, where there is doubt about penetration into the abdominal cavity, with haemodynamic instability.
3. Haemodynamic instability of unknown cause (Savoia et al. 2023).

How to perform the fast and e-fast protocol

This protocol should be carried out at the patient's bedside, avoiding their transfer to a distant cabinet unit. Likewise, it should be applied during the evaluation of circulation within the ATLS protocol's ABCDE algorithm to address the presence of free fluid and, if applicable, the possible causes of cardiac tamponade (Savoia et al. 2023).

In the thorax, FF can be found in the pericardial and pleural spaces; if the antero-superior thorax is added, it is called E-FAST or extended FAST, useful for detecting the presence of pneumothorax. It is performed using the phased array transducer (2-4 MHz) or the convex transducer (2-5 MHz) to obtain images of the right and left upper quadrants and the suprapubic regions

(Zhou and Wiley 2024). In the abdomen, the dependent spaces are susceptible to accumulating FF, such as the Morrison's space (located between the liver and the right kidney), the splenorenal space (between the spleen and the left kidney), above the spleen (subphrenic space) and within the pelvis, FF will accumulate in the pouch of Douglas. Nishijima et al. conducted a study in 2012 with the objective of systematically evaluating the accuracy and precision of symptoms, signs, laboratory tests, and bedside imaging studies for identifying intra-abdominal injuries in patients with diffuse abdominal trauma. Studies examining the identification of intra-abdominal injuries (12 studies) and a separate search for studies evaluating bedside ultrasound (22 studies) were included. It was found that the presence of intraperitoneal fluid or organ injury on bedside ultrasound evaluation is more accurate than any anamnesis and physical examination findings (LR, 30; 95% CI, 20-46%). On the other hand, in 2018, Stengel et al. conducted a Cochrane review of retrospective and prospective studies, including 34 studies with a total of 8635 patients, evaluating the diagnostic accuracy of FAST for thoracoabdominal injuries in patients with closed trauma, taking as reference standard Computed Tomography, Magnetic Resonance, laparotomy, thoracotomy or autopsy.

The primary outcome was the diagnosis of any thoracoabdominal injury; defined as free abdominal or thoracic fluid, retroperitoneum, pericardium or mediastinum, organ injury (spleen laceration, or another solid organ) as well as vascular injury (aortic dissection or injury to other vessels) and other injuries.

The results indicate that positive findings from point-of-care ultrasound can guide treatment decisions with a specificity of 0.96 and can contribute to reducing the need for imaging during trauma evaluation, especially in cases of thoracic trauma. However, for patients with abdominal and paediatric trauma, negative results from point-of-care ultrasound do not rule out injuries (with a sensitivity of 0.68 and 0.63, respectively); therefore, patients with negative results from point-of-care ultrasound require further evaluation to detect injuries (Long and April 2019).

Ultrasound for Evaluation of Thrombosis in Pelvic Limbs

Deep vein thrombosis (DVT) is part of the clinical spectrum of venous thromboembolic disease (VTE), with an incidence estimated at 1-2 episodes per 1000 people, constituting the 3rd cause of cardiovascular mortality in developed countries (Muñoz 2020).

The genesis of venous thromboembolism is multifactorial, requiring the presence of predisposing and/or triggering factors

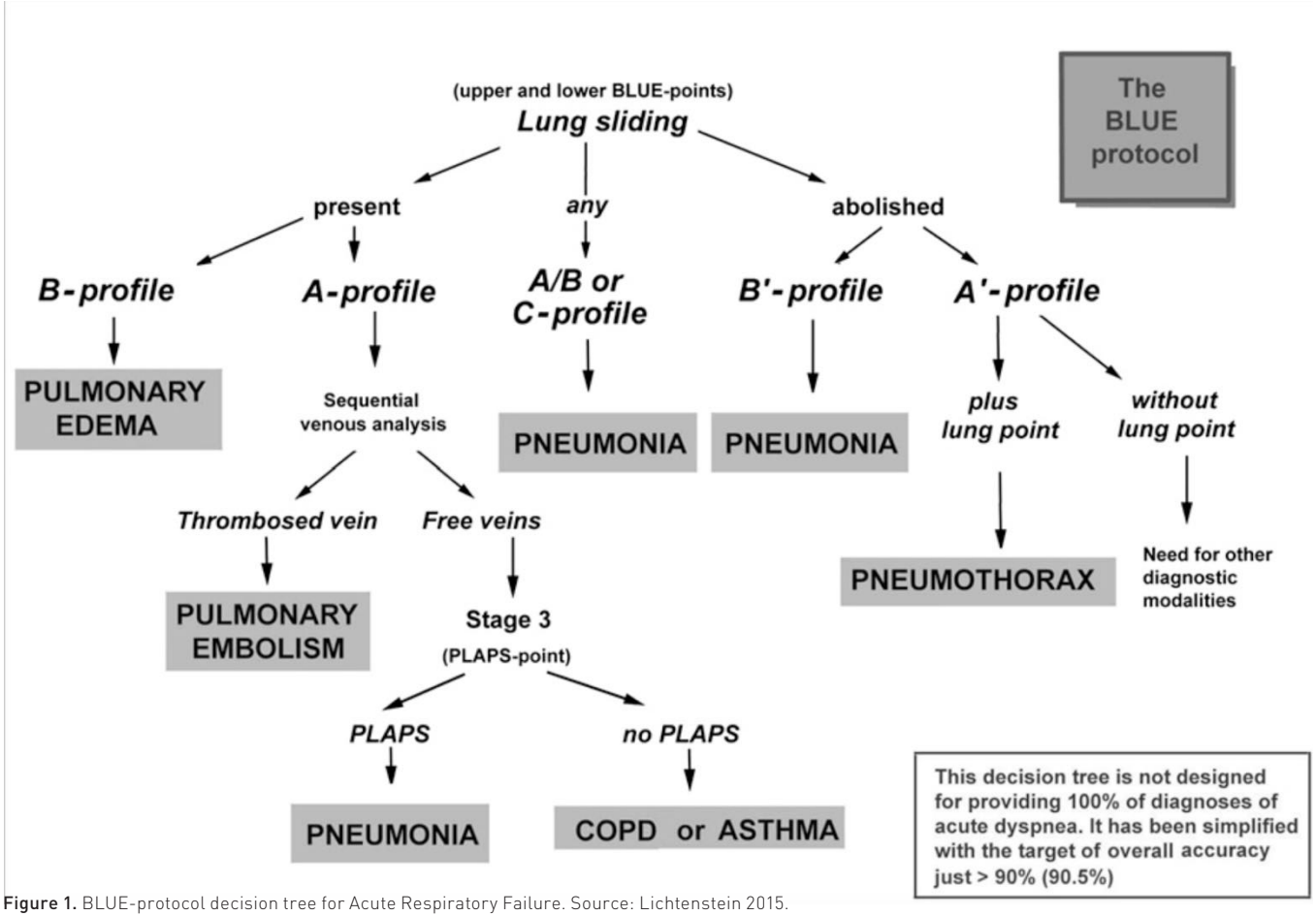


Figure 1. BLUE-protocol decision tree for Acute Respiratory Failure. Source: Lichtenstein 2015.

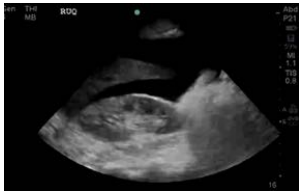
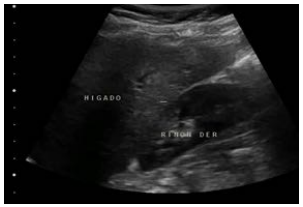
Clinical presentation	Diagnostic suspicion	Sensitivity % (95% CI)	Specificity (95% CI)	Management Strategy
Trauma patient in shock **Fast positive**	Hypovolaemic shock due to haemoperitoneum	74% (66-80%)	96% (91-98%)	Positive result: No further physical examination required.  If negative: Perform additional studies (CT, MRI). 

Table 3. Diagnostic utility of FAST examination in trauma patients presenting with shock

for its development. A prothrombotic and proinflammatory aetiology has been proposed, where coagulation factors interact with immune system cells (Khan et al. 2021). Triggering factors are associated with Virchow's Triad (venous stasis, endothelial injury, and hypercoagulability). Tissue injury leads to endothelium activation, which ultimately activates factor XII, contributing to thrombus formation (Zamarrón et al. 2021). It is crucial to achieve an accurate diagnosis of deep vein thrombosis (DVT) to prevent acute complications, such as pulmonary embolism, as well as chronic ones associated with post-thrombotic syndrome.

Diagnostic algorithms for DVT have been developed that incorporate clinical probability models based on the patient's medical history, D-dimer levels, and imaging tests. Among these tests, venous compression ultrasonography stands out as the preferred technique due to its non-invasive nature, ease of performance, and the ability to be repeated if necessary. The basic venous ultrasound examination is carried out using a linear transducer emitting medium to high frequencies (7-12 MHz). This allows for the assessment of both the femoropopliteal and distal axes, as well as the saphenous axes. Certain venous sectors may require the use of transducers with greater penetration: curvilinear transducers of low to medium frequencies (3-5 MHz), which are used to assess the iliac venous axis (Martí et al. 2023).

Five ultrasound signs that should be evaluated to diagnose venous thrombosis of the limbs are described (Kakkos et al. 2021):

1. Confirmation in B mode or grey scale of the venous lumen occupied by hyperechoic or hypoechoic material.
2. Occupation of the venous lumen by thrombotic material, leading to the most specific sign of venous thrombosis; absence of venous compressibility upon pressure with the transducer. This lack of compressibility can also be due, although without the evidence of the occupied venous lumen, to the venous plethora that may be created by obstructions proximal to the explored venous segment.
3. Venous flow is abolished in Doppler mode as in pulsed Doppler.
4. The absence of modulation or respiratory ease in the evaluation of flow at a venous point can translate into obstruction of the venous sector between the right atrium and the insonated vein.
5. The absence of an A wave increases with muscular compression in the insonated sector.

Bhatt M et al. (2020) conducted a systematic review and meta-analysis to assess the accuracy of diagnostic tests for DVT of the lower extremities in both first-time and recurrent episodes, including proximal compression ultrasound (US), whole-leg ultrasound, serial US, and quantitative high-sensitivity D-dimer assays. The review included 43 studies. For any suspected DVT, the pooled estimates of sensitivity and specificity for proximal compression ultrasound were 90.1% (95% confidence interval [CI], 86.5-92.8) and 98.5% (95% CI, 97.6-99.1), respectively. For whole-leg ultrasound, the pooled estimates were 94.0% (95% CI, 91.3-95.9) and 97.3% (95% CI, 94.8-98.6); for serial ultrasound, the pooled estimates were 97.9% (95% CI, 96.0-98.9) and 99.8% (95% CI, 99.3-99.9). The pre-test probability of DVT, often assessed by a clinical decision rule, will influence how, along with the sensitivity and specificity estimates, patients will be managed.

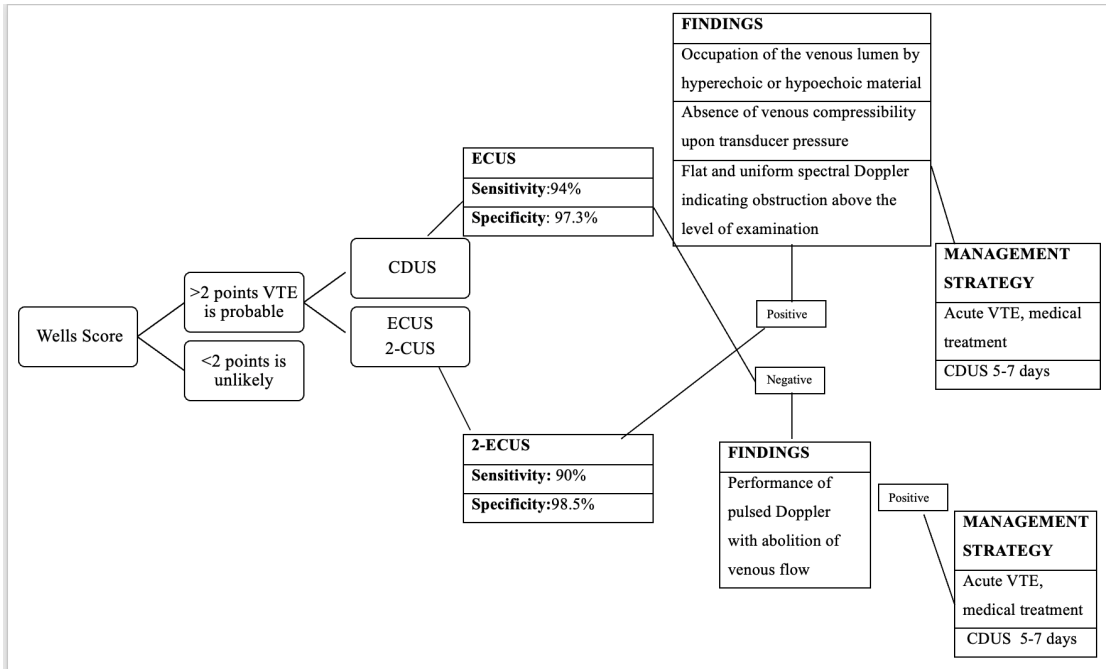


Figure 2. Algorithm for the performance of ultrasound in deep vein thrombosis and decision making. Source: Needleman et al. 2018). CDUS: Complete duplex ultrasound, 2-CUS: Two-site compression ultrasound, ECUS: Extended compression ultrasound

Conclusion

Ultrasonography proves itself as a pivotal tool in modern medical diagnostics, marked by its versatility across various disciplines. Its non-invasive, cost-effective nature, coupled with real-time imaging capabilities, makes it indispensable in settings ranging from neurocritical care to cardiology and emergency medicine. The technology's evolution continues to enhance diagnostic accuracy and safety, significantly impacting patient management and care outcomes. As ultrasound technology advances, its integration into clinical practice is expected to deepen, underscoring the need for ongoing training in ultrasonographic techniques to fully leverage this potential.

Conflict of Interest

None.

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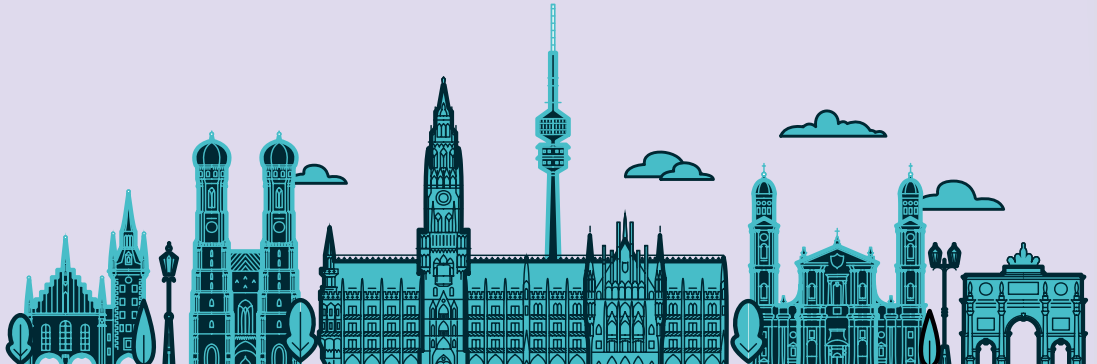

Mitral Systolic Anterior Motion: Beyond Cardiology and Cardiac Surgery

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Haemodynamic instability and shock are a potential everyday challenge for intensivists and anaesthesiologists. Understanding the underlying cause is pivotal for an appropriate and successful treatment. Systolic motion of the anterior mitral valve leaflet towards the left ventricular outflow tract (SAM) is a possible insidious mechanism of low cardiac output, severe haemodynamic instability, and hypoxaemia. All anaesthesiologists and intensivists should be aware of the mechanisms, risk factors, diagnostic features, and treatment of SAM.

Introduction

Haemodynamic instability and shock are a potential everyday challenge for intensivists and anaesthesiologists. Understanding the underlying cause is pivotal for an appropriate and successful treatment. Although cardiac output (CO) monitoring is often a first step in the management of haemodynamic instability/shock, allowing differential diagnosis between vasoplegia/distributive shock and low CO states, the causes and mechanisms of the latter can be multiple, and not all are easily recognisable if not actively researched. Systolic motion of the anterior mitral valve leaflet towards the left ventricular outflow tract (LVOT), usually more simply referred to as Systolic Anterior Motion (SAM), is a possible insidious mechanism of low CO, severe haemodynamic instability and hypoxaemia (due to dynamic LVOT obstruction and acute mitral regurgitation) requiring an echocardiographic diagnosis and a rather counterintuitive treatment (Guigui et al. 2022; Sherrid et al. 2016; Slama et al. 2016; Uematsu et al. 2017).

Although initially described as a feature of hypertrophic cardiomyopathy (HCM) (Guigui et al. 2022), SAM can also occur in the absence of pre-existing heart disease, especially in association with the haemodynamic changes which often occur in the perioperative and critical care setting, such as hypovolaemia, vasoplegia, and tachycardia (Dugar et al. 2016; Chauvet et al. 2015; Mingo et al. 2006; Abbas et al. 2019; Raut et al. 2018; Luckner et al. 2005). For this reason (and, of course, because patients with HCM may undergo surgery or be admitted to an intensive care unit for any other disease), all anaesthesiologists and intensivists should be aware of the mechanisms, risk factors, diagnostic features, and treatment of SAM.

What is Systolic Anterior Motion?

SAM is defined as the displacement of the anterior mitral leaflet (AML) towards the LVOT during systole, causing dynamic LVOT obstruction (LVOTO). It can result in mitral regurgitation (MR), reduction in CO, pulmonary oedema, hypotension, and shock (Guigui et al. 2022; Slama et al. 2016; Dugar et al. 2016; Raut et al. 2018; Cresci 2017; Duncan et al. 2023).

The mechanism of SAM is traditionally attributed to the so-called Venturi Effect, that is, the drop in pressure occurring when a fluid flows through a narrowed orifice (Pisano 2021). More precisely, what is called the Venturi Effect is the combined effect of two physical laws: the continuity equation (or Leonardo's law, after Leonardo Da Vinci) and Bernoulli's theorem (Pisano 2021). The continuity equation states that the product of the speed v of an ideal fluid flowing in a conduit and of the cross-sectional area A of the conduit itself, namely the volume flow rate Q, remains constant all along the conduit:

$$Q = A\ v = a\ constant$$

Accordingly, if the cross-sectional area decreases, the fluid speed must increase. An everyday example of this law is the increase in the speed of water coming out of a garden hose when you partially close the hose end with your thumb.

The Bernoulli's theorem is a little more complex. However, it can simply be said that when elevation changes are neglected, considering a fluid flowing along a horizontal streamline, the

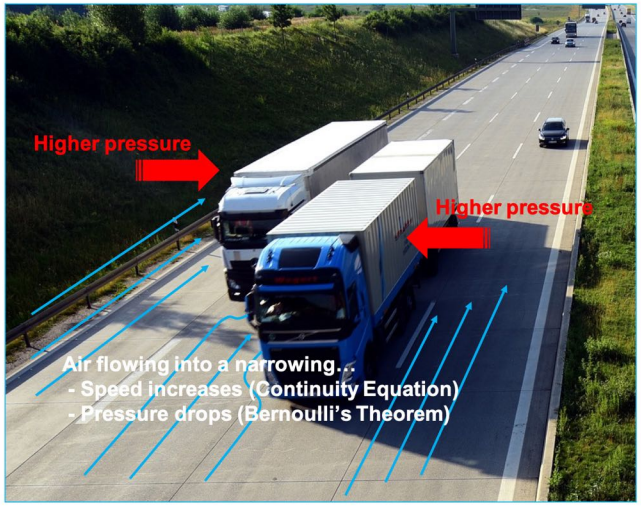

Figure 1. The Venturi Effect. According to the continuity equation, when an airflow enters a narrowing, airspeed increases and, according to Bernoulli's theorem, air pressure decreases. As a consequence, air pressure all around is higher compared to the narrowing between the two vehicles, which hence "attract" each other.

pressure is lower where the speed is higher, and vice versa. Airplanes can fly thanks to this principle (Pisano 2021).

The combined effect of these two physical laws causes that when a fluid flows through a narrowing, its speed increases (the continuity equation) and, accordingly, its pressure decreases (Bernoulli's theorem). **Figure 1** shows an example of the Venturi Effect that anyone can experience on the highway: when one vehicle comes very close to another during a high-speed overtaking, the two vehicles attract each other. In particular, if a car is overtaking a truck, it is the (lighter) car that is attracted towards the truck. A similar thing can happen in the left ventricle in the presence of all those conditions that cause LVOT narrowing or, anyway, increase blood speed through it, leading to a pressure drop which exerts a suction force dragging the AML into the LVOT towards the interventricular septum during systole (Dugar et al. 2016; Luckner et al. 2005; Pisano 2021).

Alternatively, the drag effect hypothesises that, in predisposed patients, the mitral valve (MV) leaflets are positioned in the path of LVOT flow, which drags them anteriorly and superiorly toward the septum (Dugar et al. 2016). This diastolic anterior motion of the MV may start even before the onset of systole when the velocities in the LVOT are still low (Guigui et al. 2022; Levine et al. 2014; Ro et al. 2014).

Predisposing and Precipitating Factors

Table 1 shows the predisposing (morphological) factors of SAM and all conditions that may precipitate SAM in the presence or absence of such predisposing factors.

As mentioned, SAM and LVOTO are most often observed in HCM. HCM is a rare but potentially life-threatening disease affecting around 1:200 to 1:500 individuals in the general population (Guigui et al. 2022). It is characterised by left ventricular (LV) hypertrophy without pressure overload and is a possible cause of sudden death. About 60% to 70% of patients with HCM have either resting or provocable SAM of the MV and LVOTO (Guigui et al. 2022; Cresci 2017). In HCM, reduced LV cavity dimensions, myocardial hypertrophy, and increased LV contractility are all factors that increase blood speed in the LVOT during systole, predisposing to SAM. More generally, global or isolated (septal) hypertrophy represents a predisposing factor for SAM: while a diastolic ventricular septum thickness >15 mm is considered diagnostic for HCM (Uematsu et al. 2017; Cresci 2017), a sigmoid septum is regarded to as a risk factor for SAM also in patients without HCM (Uematsu et al. 2017).

However, SAM has been described in patients with or without myocardial hypertrophy in a variety of clinical settings, such as general or neuraxial anaesthesia (Chou 2022; Fujita et al. 2015; Hussey et al. 2023; Monaco et al. 2022; Essandoh et al. 2016), cardiac surgery (particularly after MV repair or aortic valve replacement) (Weich et al. 2021; Makhija et al. 2019; Ashikhmina et al. 2021), myocardial infarction (Mingo et al. 2006), septic shock (Chauvet et al. 2015; Mingo et al. 2006; Abbas et al. 2019; Balik et al. 2020), use of inotropic medications (Mingo et al. 2006), exercise or dobutamine stress test (Alhaj et al. 2013), and anaphylaxis (Nooli et al. 2023). Finally, dynamic LVOTO has also been described in the acute phase of Tako-Tsubo cardiomyopathy (Yasuhiro et al. 2022; Di Vece et al. 2021; Conradi et al. 2021). In all these clinical settings, one or more factors, including hypovolaemia, vasodilation, increased heart rate, and increased inotropism (Dugar et al. 2016), may contribute to increasing blood velocity through the LVOT and, hence, to SAM development.

SAM in the Intensive Care Unit and Perioperative Setting

Intensive Care Unit (ICU) patients, as well as patients undergoing surgery, are particularly exposed to haemodynamic changes that may increase blood velocity through the LVOT, possibly leading (or contributing) to SAM development, such as hypovolaemia (e.g. acute blood loss), vasodilation (e.g. distributive shock, neuraxial anaesthesia, use of vasodilator drugs), tachycardia (e.g. compensatory, pain, fever, anxiety), or increased LV contractility (e.g. use of inotropic drugs, hyperdynamic shock) (Slama et al. 2016). However, reports of haemodynamic instability/shock due to SAM in these settings are mostly limited to case reports or small case series.

SAM in ICU patients

Dynamic LVOTO is a potential cause of severe haemodynamic instability, despite volume optimisation and use of vasoconstrictors, in patients with septic shock (Dugar et al. 2016; Chauvet et al. 2015; Balik et al. 2020; Evans et al. 2021). Among 218 patients admitted to ICU due to septic shock, Chauvet et al. (2015) reported the presence of echocardiographic signs of left intraventricular

Morphological	Functional
Thickening of the interventricular septum narrowing the LVOT	Hypovolaemia
Elongation of mitral leaflets	Tachycardia
Post-surgical-correction elongation of the MV leaflets or annular undersizing or complete ring annuloplasty in MV repair	Reduced preload
Morphological alterations or atypical insertion of papillary muscles	Reduced afterload, vasodilation
Aortomitral angle <120°	Increase contractility
Minimum distance from the coaptation point to the septum (C-Sept) < 2.5 cm	
Chordal anomalies or surgical chordal interventions	

Table 1. Predisposing and precipitating factors of LVOTO and SAM. *LVOTO, left ventricle outflow tract obstruction; SAM, systolic anterior motion; LVOT, left ventricle outflow tract; MV, mitral valve*

dynamic obstruction in 22% and found that this occurrence was associated with higher 28-day mortality. However, Balik et al. (2020) found severe LVOTO (including SAM) in only 10 out of 527 septic shock patients. Other authors reported SAM as the main mechanism of severe shock in septic patients without pre-existing heart disease, possibly due to vasodilation/tachycardia/increased LV contractility associated with sepsis (e.g. Dugar et al. 2016). In other cases, the occurrence of SAM in two ICU patients was attributed to an excessive use of catecholamines (Mingo et al. 2006).

A poor response to treatment with inotropic agents and/or mechanical circulatory support after myocardial infarction should always prompt echocardiographic evaluation in order to rule out LVOTO, which can mimic cardiogenic shock: also in this case, hypercontractility of non-ischaemic regions, changes in LV chamber size, and tachyarrhythmias (e.g. following catecholamine administration) can lead to dynamic LVOTO (Mingo et al. 2006; Harrington et al. 2023).

Finally, dynamic LVOTO has been described in the setting of neurosurgical ICU in two patients treated with milrinone (an inodilator) for cerebral vasospasm, with confirmed SAM in at least one of the two cases (Baulier et al. 2022).

SAM in the perioperative setting

Dynamic LVOTO/SAM is a well-known phenomenon to cardiac anaesthesiologists. After cardiac surgery, it can especially occur following aortic valve replacement (AVR) or MV repair (MVR). In patients undergoing AVR, in addition to the factors mentioned above such as LV septal hypertrophy, use of inotropic medications, hypovolaemia, and vasodilation, further predisposing factors include the use of intra-aortic balloon pump (IABP), MV abnormalities, and concomitant MV replacement with a high-profile bioprosthetic valve (Makhija et al. 2019; Huang 2024). Similarly, SAM has been reported after transcatheter aortic valve replacement (TAVR) (Weich et al. 2021; Ben-Dor et al. 2022).

SAM can occur in up to 13% of patients undergoing MVR (Ashikhmina et al. 2021), particularly in those with LV ejection fraction (LVEF) > 60%, excessive height of the MV leaflets (particularly of the posterior one), or who received complete ring annuloplasty (Loulmet et al. 2014). Moreover, bi-leaflet prolapse, a low ratio of the heights of the anterior to posterior MV leaflets, low end-systolic LV volume, and younger age at the time of surgery are reported as risk factors for SAM after MVR (Ashikhmina et al. 2021).

However, many reports of SAM in patients undergoing noncardiac surgery also exist. Luckner et al. (2005) reported the occurrence of severe perioperative hypotension due to SAM in three patients undergoing orthopaedic surgery for bilateral femoral neck fracture, cholecystectomy with hepatic resection for gallbladder carcinoma, and femur prosthesis for repeated hip prosthesis dislocations, respectively. None of the three patients had anatomical predisposing factors for SAM, while hypovolaemia and anaesthesia-induced vasodilation were regarded to as the main precipitating factors in all three cases. Other authors reported SAM during thoracoscopic surgery (Monaco et al. 2022), liver transplantation (Essandoh et al. 2016), kidney transplantation (complicated by anaphylaxis following antibiotic administration) (Nooli et al. 2023) and, in general, due to a decrease in preload and/or increase in heart rate secondarily to general or neuraxial anaesthesia (Chou 2022) or pneumoperitoneum (Fujita et al. 2015).

Diagnosis and Management

Unexpected severe hypotension is the most common manifestation of SAM in ICU or surgical patients (Luckner et al. 2005). However, hypoxaemia due to mitral regurgitation and pulmonary oedema has also been reported as a possible clinical presentation (Chou 2022; Fujita et al. 2015). Severe haemodynamic instability (particularly which worsens by administering or increasing the doses of inotropes), a progressive increase in norepinephrine

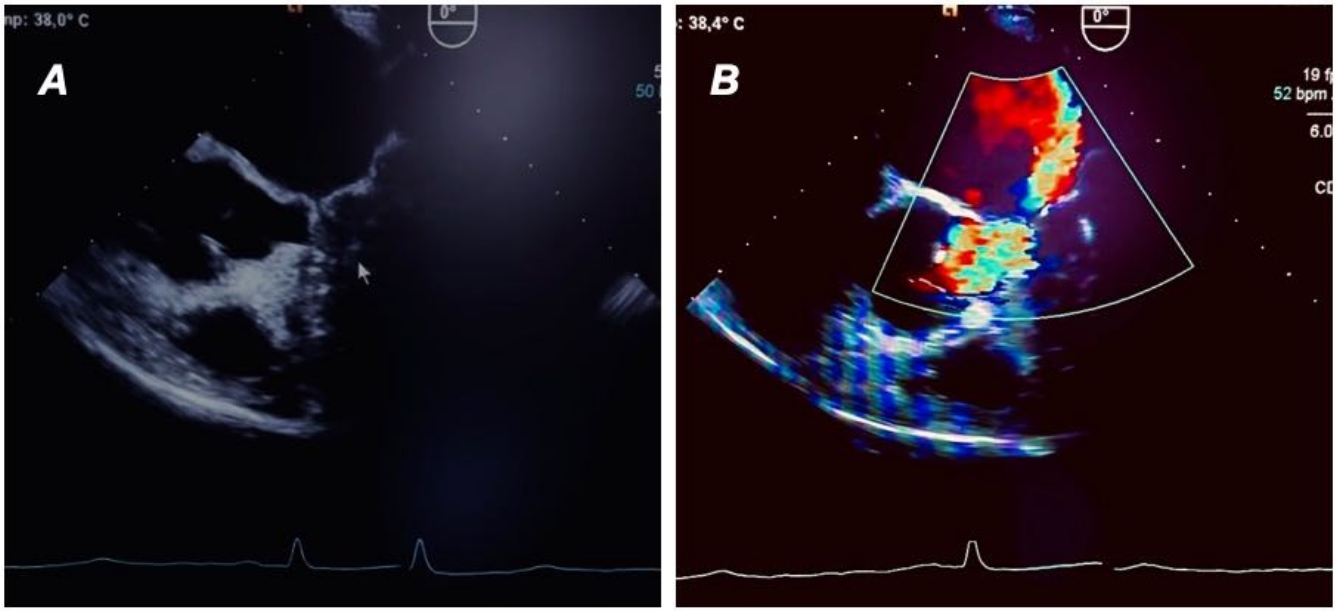

Figure 2. Two-dimensional transoesophageal echocardiography showing mitral valve systolic anterior motion (SAM) as mid-systolic contact of the mitral valve anterior leaflet with the septum (A) and turbulence (mosaic flow signal) at the site of SAM-septal contact with a concomitant eccentric mitral regurgitation jet at the colour flow Doppler analysis (B).

requirements, and worsening oxygenation should prompt cardiac ultrasound examination in order to rapidly differentiate among cardiogenic shock due to impaired ventricular function, distributive shock, and LVOTO/SAM (Duncan et al. 2023).

Cardiac ultrasound examination

Main echocardiographic findings in patients with LVOTO/SAM include a crescent shaped LV cavity, normal or slightly supernormal LVEF, asymmetrical septal hypertrophy (ASH) with wall thickness >1.5 cm in basal anteroseptum (Cresci 2017); LVOTO is dynamic and variable with loading conditions, with an outflow gradient > 30 mmHg (velocity >2.7 sec); SAM is visible as the mid-systolic contact of the MV anterior leaflet with the septum (particularly in M-mode) (Guigui et al. 2022), while colour flow Doppler reveals turbulence (mosaic flow signal) at the site of SAM-septal contact (Raut et al. 2018) (**Figure 2**); in most severe cases, closure of the aortic valve due to reduced sub-valvular pressure can occur; MR secondary to SAM is characterised by an eccentric posteriorly directed jet due to failed apposition of mitral leaflets, unlike the central or anteriorly directed jet which is typical of primary MV disease (Guigui et al. 2022). Further descriptions of the anatomical/echocardiographic features of HCM are beyond the scope of the present review and can be found elsewhere (Guigui et al. 2022; Sherrid et al. 2016).

Prevention and Treatment

Medical management of SAM in HCM patients includes chronic therapy with beta-blockers and calcium antagonists (mostly verapamil) to improve LV filling and volume loading and avoid afterload reduction (Guigui et al. 2022; Maron et al. 2018).

Mavacamten, a myosin adenosine triphosphatase inhibitor, was shown to improve symptoms, exercise capacity, and LVOTO, as well as SAM and important measures of LV diastolic function and biomarkers of myocardial wall stress in a randomised controlled trial (RCT) of 251 patients with symptomatic (obstructive) HCM (Hegde et al. 2021; Olivotto et al. 2020). To our knowledge, this is the only RCT involving patients with SAM. In HCM patients with refractory obstruction and persistent symptoms despite medical therapy, surgical septal myectomy should be preferred, particularly in younger patients, while percutaneous alcohol septal ablation is a reasonable alternative in higher-risk patients; MV surgery is generally indicated for patients with mild to moderate septal hypertrophy, intrinsic MV disease, or papillary muscle abnormalities (Guigui et al. 2022; Affronti et al. 2021).

In patients with HCM or isolated (septal) hypertrophy, the anaesthetic strategy should be carefully evaluated. Although neuraxial anaesthesia was historically considered contraindicated, selective techniques which avoid excessive vasoplegia could probably be performed, taking the possibility of SAM into consideration and preventing hypovolaemia. The choice of the anaesthetic regimen can be particularly challenging in conditions in which general anaesthesia represents an issue, such as during pregnancy (Hussey et al. 2023). Anaesthesiologists should also consider peripheral nerve blockades over neuraxial anaesthesia to avoid vasodilation (Monaco et al. 2022).

In light of the pathophysiology discussed above, the cornerstones of acute treatment of severe shock due to SAM in the critical care or perioperative setting are fluid resuscitation, use of vasoconstrictors (pure vasoconstrictors such as phenylephrine or vasopressin may be preferable to norepinephrine), and discontinuation of inotropic (and vasodilating) agents; moreover, β-blockers and/or calcium channel blockers (verapamil) can be used to decrease heart rate and cardiac contractility (Dugar et al. 2016; Mingo et al. 2006; Abbas et al. 2019; Duncan et al. 2023; Makhija et al. 2019; Poveda-Jaramillo et al. 2018). Particularly in the setting of myocardial infarction, discontinuation of IABP

mechanical support should also be considered (Harrington et al. 2023), while especially after cardiac surgery, atrial pacing can be useful as the conversion from normal sinus rhythm to junctional rhythm can worsen SAM, possibly due to the lack of the atrial kick (Seino et al. 2018).

Administration of vasopressin has been shown to significantly reduce norepinephrine requirements, improve haemodynamics, and reduce the severity of MR and pulmonary oedema in septic shock patients with SAM (Balik et al. 2020).

The ultra-short-acting selective β-blockers (esmolol, landiolol) should be preferred for the management of heart rate and arrhythmias in septic patients due to their safety and simplicity of use (Poveda-Jaramillo et al. 2018). In cardiac surgery, e.g. following MV repair, the lack of response to esmolol administration has been proposed as a strategy to identify patients with SAM who may be not responsive to conservative therapy, needing surgical revision (Poveda-Jaramillo et al. 2018; Landoni et al. 2011).

Conclusion

Although usually associated to the setting of HCM and cardiac surgery, SAM can also occur in the absence of pre-existing heart disease, especially in association with the haemodynamic changes which often occur in the perioperative and critical care setting, such as hypovolaemia, vasoplegia, increased heart contractility, and tachycardia. Accordingly, all intensivists and anaesthesiologists should be aware of the pathophysiology, risk factors, and correct management of SAM and actively seek it out (with echocardiography), particularly in the presence of severe haemodynamic instability which worsens with the increase in inotropic drug doses. This condition can mimic fluid overload and cardiogenic shock, and treating it with diuretics, vasodilators, and inotropic drugs leads to a progressive worsening in haemodynamics, hypoxaemia and shock or sudden death.

Conflict of Interest

None.

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Taking Care of the Lung Donor: A Task For Every Hospital

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Every hospital can contribute to adequate lung donation. Learning and understanding the management of potential donors will allow them to receive proper care and be referred to save a life.

Introduction

Organ transplants are, in many cases, the only therapeutic option for patients with terminal diseases in different organs (Westphal et al. 2016). There is a marked imbalance between the number of available organs and the number of potential recipients (McKeown et al. 2012). In the U.K., U.S. and Europe, the number of potential transplant recipients has risen to more than 133,000, while the number of organs donated from all sources is not increasing enough to keep up with this growth rate (Klein et al. 2010).

Lung transplantation is a treatment option for people with terminal lung diseases despite the maximum medical treatment available. The number of transplants is limited by the shortage of organs, which generates high mortality on the waiting list. In Mexico, the population of patients with lung involvement likely to need a lung transplant is high. Chronic obstructive pulmonary disease (COPD) has a prevalence of 7.8% in the adult population. In idiopathic pulmonary fibrosis (IPF), an estimated annual incidence of up to eight cases per 100 thousand habitants is described (Moisés Acuña-Kaldman 2016; Monserrat Martínez Luna 2020).

According to data from the World Health Organization (WHO), our current health situation in relation to the COVID-19 pandemic, Mexico stands out as the seventh country with the most confirmed cases and the fourth with the most deaths, surpassing countries with a considerably higher population rate such as USA, Brazil and India (WHO 2023).

The urgent need to maintain lung transplant activity despite the pandemic is very clear, given the responsibility in our country to respond to the more than 20,000 patients waiting for an organ transplant. The National Centre of Transplants implemented on September 25, 2020 a coordinated gradual reactivation plan based on the control of the SARS-CoV-2 (COVID-19) epidemic in each federal entity (José Salvador Aburto-Morales 2020).

As in other parts of the world, the lack of donors in Mexico is a big problem. This, combined with multiple other factors, such as the lack of centres with adequate training and the cost, have prevented this procedure from being consolidated (Santillan-Doherty et al. 1993). Despite this, the first successful lung transplant for COVID-19 in Latin America was performed in Mexico by the only active group to date in this country (Wong-Jaén 2020).

Between April 2017 and December 2023, this lung transplant group performed 36 transplant procedures, 75% of them being two-lung. Twenty-five patients were men, and in 21 of the thirty-six patients, the diagnosis was idiopathic pulmonary fibrosis. Survival at 12 months was 78%, and at 90 days, it was above 85%.

The greatest challenges for lung transplantation in Mexico are not different from those faced by programmes in neighbouring countries with similar socioeconomic characteristics. It is vital to increase the rate of effective lung donation, increase the number of lung transplant programmes and overcome the learning curve.

Just to contextualise, it is known that in the best of scenarios, 40% of multi-organ donors will be able to effectively donate the lung (Klein et al. 2010). In relation to the population (130 million inhabitants), in 2019 Mexico exhibited an average global rate of organ donation due to brain death per million inhabitants of 4.5 (0.3 - 14.2), which as a result of the Sars Cov2 pandemic decreased for 2022 at 3.4 (0.5 - 11.1), a clearly low rate (CENATRA 2023).

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Identification of the Multi-Organ Donor

Considering the shortage of organs available for transplant, it seems essential to inform every doctor who is dedicated to the care of critically ill patients that they have the tools for early identification and adequate and timely management of the potential donor in the areas that care for patients in critical condition, and not only in intensive care units (ICU) (van Zanden et al. 2019).

Any emergency room or intensive care unit can potentially house the next donor candidate. The prompt identification and adequate care of the potential donor is a task that any doctor who cares for critical patients (emergency doctor, intensivist, etc) must be able to carry out (Ismail et al. 2023). The fact that the hospital in question does not have a transplant or procurement programme is not a limitation in identifying potential donors through the Glasgow <7 programme (Bustos et al. 2006).

Glasgow <7 Programme

One-third of patients with Glasgow <7 progress to the criteria to be organ donors (Vanholder et al. 2021). Another third progresses to cardiopulmonary arrest, which makes them candidates to be tissue donors; the rest evolve towards improvement (Schoene et al., 2023). In any scenario, it is essential to provide adequate multiorgan support, in addition to establishing a neurological evaluation that includes performing a neurological window (Neitzke et al. 2019; Aulisio et al. 2007; Mizraji et al. 2009). Contrary to what one might think, starting these evaluations does not lead to a scenario of suspending support or preventing recovery scenarios (Aulisio et al. 2007). All three scenarios imply adequate care of the patient. What we are trying to avoid is the scenario where the support is suspended without considering the possibility that the patient may be a candidate for donation. If the patient is potentially a candidate for donation, a preliminary apnoea test without disconnection from the ventilator can be performed (Del Rio et al. 2009). If this test raises the possibility of the patient being a donor, it is important to contact the procurement centre (if the patient is not in one already) and discuss the possibility of transfer with the intention of increasing the patient's level of support and defining if the evolution will be towards improvement, or if the evaluation towards a potential donor can continue (Imaoka et al. 2023; Vail et al. 2023). While it is established if a patient in Glasgow <7 protocol evolves to any of the three previous scenarios, it is essential to maintain adequate multi-organ support (Messer et al. 2023).

General Non-Pulmonary Management of the Multi-Organ Donor

Haemodynamic

In a possible donor candidate, the main cause of hypotension is directly related to the cause of admission, and in most cases is hypovolaemia. This is where a balance must be found between aggressive resuscitation and fluid overload (ELAyashy et al. 2019; Marklin et al. 2023).

Hypotension is multifactorial (Chudoba et al. 2017). It is caused primarily by vasodilation associated with loss of vasomotor tone or spinal cord shock. Patients may also present hypovolaemia due to severe polyuria caused by diabetes insipidus or hypothermia. Finally, there may be hypotension of cardiogenic origin due to bradyarrhythmias or related to sepsis. Therefore, haemodynamic monitoring is mandatory for the appropriate differential diagnosis (Shah 2008; Darby et al. 1989).

Minimal monitoring (Rudnick et al. 2015; Kim et al. 2022b) requires measurement of the central venous pressure (CVP) and arterial line. It is desirable to maintain a target CVP >5 and <8 mmHg. In patients with great instability or high fluid need, monitoring of pulmonary artery pressure and cardiac output by thermodilution is recommended, especially for diagnosis and management of hypotension with vasopressors, volume and/or inotropes (Vieira and Carmona 2020). Pulmonary extravascular water can be monitored with a PiCCO catheter, maintaining <10 ml/kg ideal weight (Li et al. 2021). A non-invasive option is the use of lung ultrasound with the measurement of B lines maintaining an ultrasound extravascular water scale of less than 4 points (Lebovitz et al. 2016; Lindow et al. 2023). In the scenario of a possible donor candidate, the placement of a central venous catheter should never be an emergency; the initial resuscitation can be carried out via a peripheral catheter with enough time to plan the placement of a central access guided by ultrasound by an experienced provider (van der Mee-Marquet et al. 2023; Ouerd et al. 2023). In the case of diabetes insipidus or hypotension due to hypovolaemia caused by intense polyuria, resuscitation should be performed with hypotonic solutions or glucose solutions to reduce hypernatraemia (Opdam 2019; Meyfroidt et al. 2019; Kazemeyni and Esfahani 2008). In any other case, the use of balanced solutions is appropriate (Semler and Kellum 2019).

Endocrine

Once the criteria for brain death have been established, the initiation of steroids (15 mg/kg of methylprednisolone) should be considered due to the resulting pituitary adrenal insufficiency (Kuhn and Hahnenkamp 2019). There is no consensus on whether

all cases require thyroid hormone replacement or the exact time for its initiation (Novitzky et al. 2014). Diabetes insipidus is prevalent during brain death and should be treated primarily with nasal desmopressin or vasopressin infusion based on urine output and serum sodium (Valenza et al. 2014).

Most consensuses propose serum glucose levels of the potential donor between 150 to 200 mg/dl. Glycaemic control will be complicated in the potential donor, especially if high doses of steroids are administered (Lagiewska et al. 1996). Only 1 in 4 donors will have glucose <200 mg/dl, and levels >250 mg/dl have been associated with failure in the donation process at some point. Another factor to keep in mind is that insulin doses can be >30 units/hour, especially in cases where steroid/thyroid hormone therapy is started or when hypotonic glucose solutions are used (Marvin and Morton 2009).

Haematologic

The ideal haemoglobin level for optimising oxygen transport to the organs to be transplanted is 10 g/dl (Kim et al. 2022a). Coagulation disorders and thrombocytopenia are common and worsen if there is hypothermia. They must be corrected according to the abnormality detected (Powner et al. 2011).

Thermal control

Normothermia is important for organ preservation. Furthermore, hypothermia causes vasodilation with hypotension, arrhythmias and coagulation disorders. Therefore, body temperature should always be maintained above 35 degrees Celsius with appropriate physical means (Wright et al. 2019).

Lung Donor

Lung donation represents greater difficulty than obtaining other solid organs due to several factors (Okahara et al. 2022):

a. Lungs are the largest solid organs that are transplanted and are in direct contact with the atmosphere and, at the same time, with all the blood in the body.

b. The condition of brain death is frequently due to multiple trauma, in which the possibility of chest trauma or bronchoaspiration is highly prevalent.

c. The multi-organ donor in brain death is necessarily on mechanical ventilation with an artificial airway in an intensive care unit. The possibility of ventilator-associated pneumonia may make the lungs unsuitable for transplant.

Traditional lung donation candidate selection criteria are listed below (Chaney et al. 2014):

- Age < 55 years
- ABO blood type compatibility (RH compatibility is not necessary)
- Chest x-ray without opacities (rule out atelectasis)
- PaO_2/FiO_2 ≥300 with FiO_2 100% PEEP 5 cmH_2O after 20 min
- Smoking history < 20 pack years
- No history of chest trauma
- Minimal risk of aspiration or sepsis
- No history of cardiothoracic surgery
- Gram-negative bronchial secretion
- Absence of purulent secretions on bronchoscopy

More than half of current donors worldwide do not meet half of these criteria. Thus, extended donor criteria have been proposed, and the success of these cases appears to be similar to that of candidates who meet the traditional criteria. In these cases, communication with a transplant expert is necessary to define whether the case is a candidate to be an extended donor and not rule out any potential donor (Minambres et al. 2016). **Table 1** shows the extended criteria that have shown a very similar long-term evolution in patients transplanted from marginal donors. Many of them can be rescued based on protocols that optimise the organs, which are shown below (Lesko and Angel 2023; Botha et al. 2006).

On the other hand, the anthropometric characteristics between donor and recipient should be compared (Ogunlana et al. 2021), with the most used formula being the prediction of total lung capacity (TLC) see formulas 1 and 2 (Barnard et al. 2013):

Indicator	Ideal donor	Standard criteria	Marginal donor	Rejected donor
Age (years)	20-45	<55	60-65	
PO_2/FiO_2 (mmHg)	>350	<300	Optimisation	200
Smoking history	Never	<20 packages /year	Cumulative – Recent	¿?
Radiography	Clear	Clear	Infiltrates – Optimisation	Dense condensation
Microbiology	Negative culture	Gram-negative	Antibiotics	Resistant microorganisms
Bronchoscopy	Clear	Non-purulent	Purulent - ¿Aspiration?	Tumour

Table 1. Standard and extended criteria for lung donation. Source: Botha et al. 2006

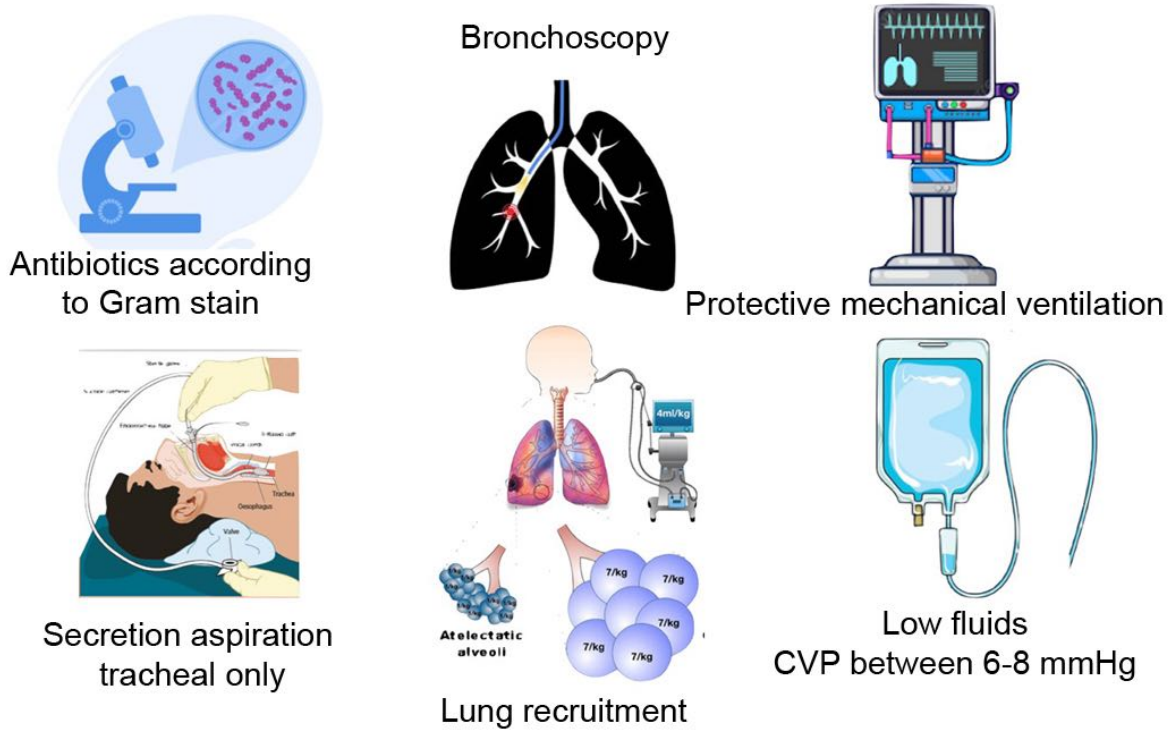

Figure 1. Lung donor care measures

Women:

TLC = (7.99 * m) – 7.08

Men:

TLC = (6.6 * m) – 5.79

where: m = stature in metres

The donor and recipient must share between 75-125% of the CPT. This range is very wide due to the recipient's ability to adapt the thoracic cavity to the new lung. However, in complex cases when the recipient's thoracic cavity is too small, graft reduction adjustments should be evaluated. The primary recruitment centres for potential donors will not carry out the comparison, but this is very important information that the transplant group must have in the initial evaluation data of the case (Ouwens et al. 2002). Another widely used method is to use chest measurements, which are possible with digital imaging equipment, between the recipient's x-ray and the donor's x-ray.

In lung transplantation, ABO blood group compatibility is necessary. There is no difference in the results when compatible and non-identical donors are used, such as in blood transfusion. Rh compatibility is not considered in lung transplantation (Chen-Yoshikawa 2023).

Regarding ischaemia time, the time from the donor's aortic clamping to begin procurement until the restart of reperfusion in the transplanted lung should be around six hours, an important logistical aspect to consider the procurement, transfer and implantation time. Only a third of cases worldwide report these times (Meyer et al. 2000).

Care of the Lung Donation Candidate

If an adequate care protocol is not established, especially regarding mechanical ventilation, donation candidates may only be accepted in <25% of cases, while if appropriate care is applied, 1 in 2 candidates may be procured (Shepherd et al. 2021).

Fluid management is crucial in pulmonary procurement. Unlike other organs such as the kidney, lungs suffer damage such as inflammation and oedema if there is any excess in body volume. The haemodynamic monitoring methods to achieve this objective have already been mentioned in previous sections.

Patients should be managed ventilatorily with lung protection criteria. The tidal volume should be 6-8 ml/kg of ideal body weight with the minimum FiO_2 that maintains appropriate oxygen saturation. The PEEP level can be set between 5 and 8 cmH_2O. Patients can be managed in pressure or volume mode with an appropriate respiratory rate to maintain normal pH and pCO_2.

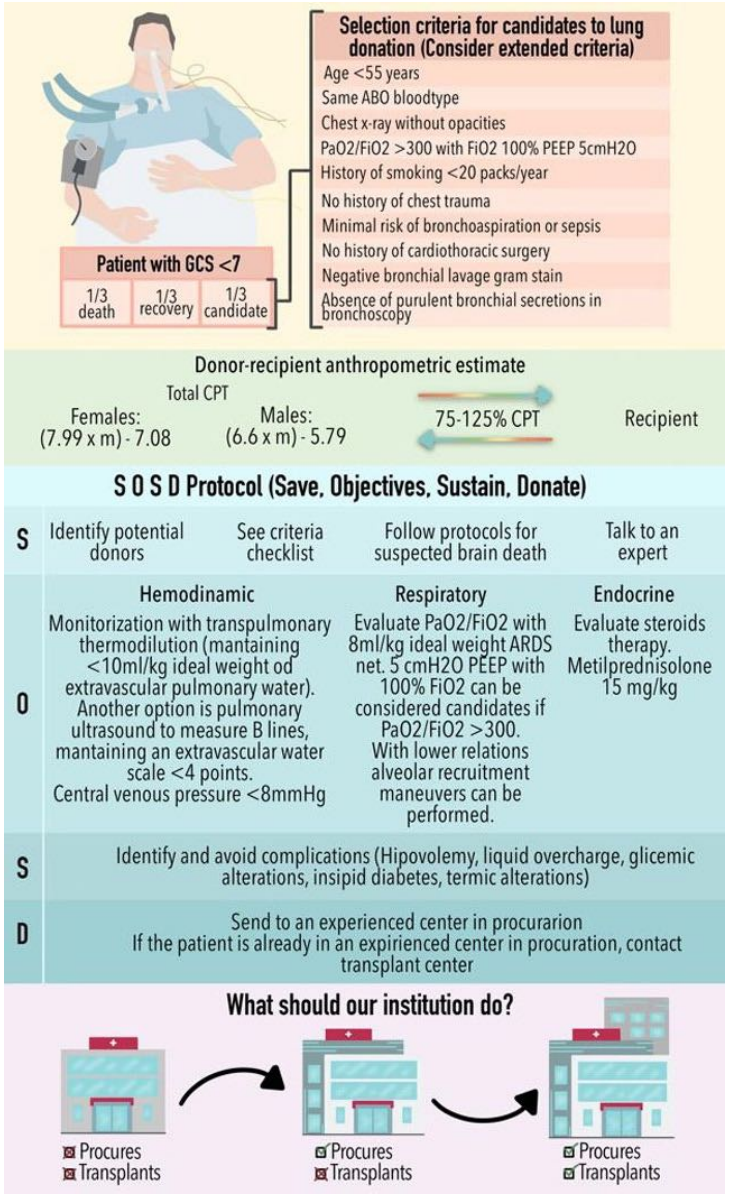

Figure 2. Infographic of the care process of the lung donor candidate

It is extremely important that during aspiration of secretions there is no desaturation using a closed aspiration system. Aspirate only if there are secretions and avoid inserting the aspiration catheter beyond the carina.

It will always be desirable to perform a bronchoscopy on the donor. This procedure helps cleaning the airway and bronchi. In addition, it helps to evaluate if there is evident infection of the airway and lung parenchyma. It is normal to find purulent secretions in the bronchi that may mean bronchitis. However, if bronchoscopy detects distal secretions that continue to be aspirated continuously, this suggests that there may be distal infection or pneumonia, which rules out that lung for donation (**Figure 1**).

Different rescue protocols for marginal lungs have been published. The reasoning behind these protocols is to maximise lung function through fluid management and bronchial cleansing by bronchoscopy, in addition to the use of alveolar recruitment manoeuvres with mechanical ventilation. Thus, there are lungs that may not have acceptance criteria for lung transplantation but can be optimised or rescued with these protocols. The first publication in this regard is the "SALT" protocol from the group at the University of Texas at San Antonio (Angel et al. 2006). The suggested recruitment is to place the patient in a pressure mode on the ventilator, with PEEP of 15 cmH_2O and cycling pressure of 15 cmH_2O. Some lungs can improve their pO_2/FiO_2 ratio with this management in addition to bronchoscopy and fluid optimisation.

Very recently, ex-vivo perfusion has been proposed using perfusion and extracorporeal ventilation for a few hours to rescue these lungs, even using antibiotic therapy in case of infection (Sommer et al. 2013; Snell et al. 2018).

Conclusion

Figure 2 shows an infographic with a summary of all the points discussed here. It is based on the SOSD mnemonic, which is useful to consider all aspects of multi-organ donation with a focus on the lung donor. There are very few hospitals that have the capacity to have a lung transplant programme. Hospitals with the capacity to procure organs are not sufficient for the number of donors required. Therefore it is important that all hospitals can accommodate a potential donor, and it is important that all potential donor candidates can have an adequate evaluation and, if applicable, they can be integrated into a donation programme. If your hospital does not have a procurement programme, Glasgow <7 patients should be identified and proposed to be sent to a centre with experience and authorisation for organ procurement.

If it is a procurement centre, the evaluation of the potential candidate must be completed, and a lung transplant programme and a centre with experience in organ transplantation must be contacted. Time is vital since brain death has a time window limited to a few days. Organ donation should be part of any hospital. This way, the organ procurement rate in our country can be improved, thus benefitting thousands of patients who would have the opportunity to receive the gift of life.

Conflict of Interest

None.

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https://iii.hm/1pzr

ICU MANAGEMENT AND PRACTICE IS PUBLISHED BY
MindByte Communications Ltd
Kosta Ourani, 5 Petoussis Court, 5th floor, CY-3085 Limassol Cyprus
Email office@icu-management.org
Website icu-management.org

SUBSCRIPTION RATES
One year 55 Euros + 5% VAT if applicable
Two years 90 Euros + 5% VAT if applicable
Note: For a free digital subscription please contact Samna Ghani, editorial@icu-management.org

PRODUCTION, FULFILMENT AND DISTRIBUTION
Total distribution: 21,500
ISSN = 1377-7564

VERIFIED CIRCULATION
according to the standards of International Business Press Audits.

ICU Management & Practice is independently audited by Top Pro CY.

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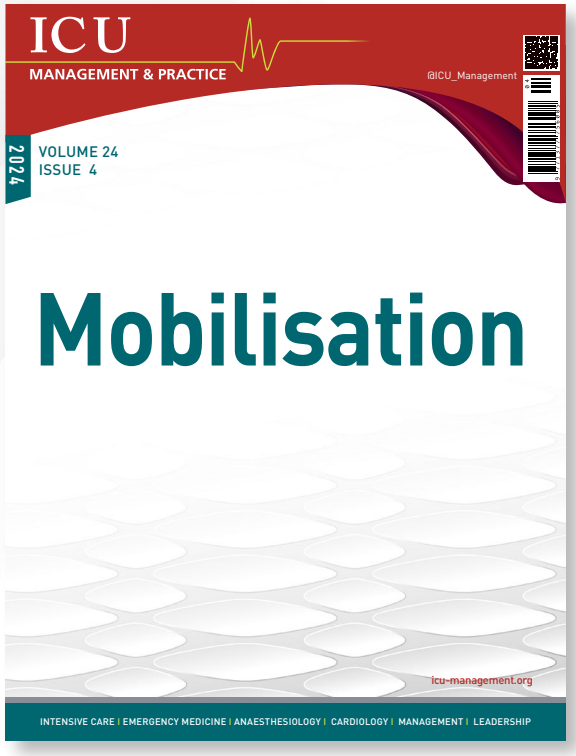

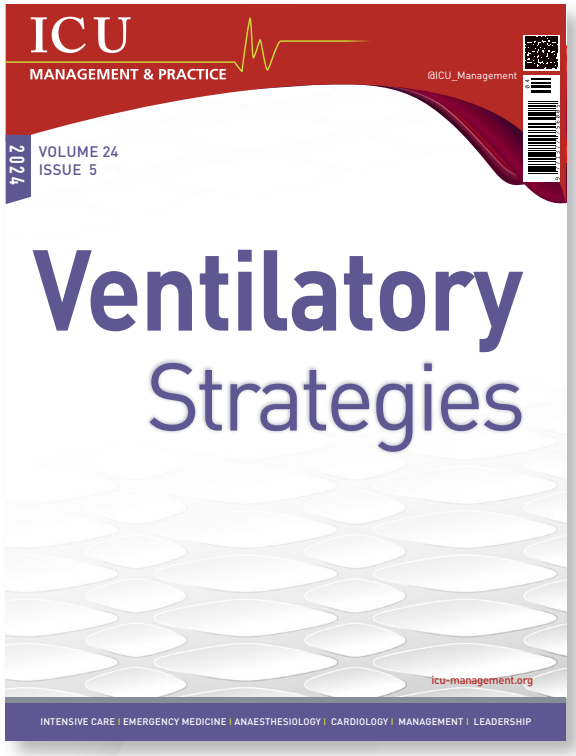

COVER STORY: Mobilisation

Mobilisation is an essential aspect of the care for patients in the ICU. In this issue, our contributors discuss the importance of mobilisation for ICU patients and how the critical care team can effectively plan and execute an early mobilisation strategy while considering the patient's condition and recovery.

COVER STORY: Ventilatory Strategies

Ventilatory strategies are critical for managing patients in the ICU. In this issue, our contributors discuss ventilation strategies, lung mechanics, and individual response to treatment while ensuring optimised oxygenation, minimum ventilator-associated lung injury, and effective weaning from mechanical ventilation.

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