

CRITICAL ROUNDS



MICRO LABS LIMITED

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Dear Doctor,

Greetings from Micro Labs limited. We are happy to bring **"CRITICAL ROUNDS"** containing latest information in the field of Critical care medicine.

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Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

Looking forward to your valuable feedback

Best Regards,
Medical Team, Micro Labs Ltd

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Antifungal prophylaxis for prevention of COVID-19-associated pulmonary aspergillosis in critically ill patients: An observational study

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) disease 2019 (COVID-19)-associated acute respiratory failure contributes to a highly permissive inflammatory environment, which in turn favours fungal pathogenesis due to the release of danger-associated molecular patterns and collateral effects of host recognition pathways required for the activation of antiviral immunity. COVID-19-associated pulmonary aspergillosis (CAPA) has been emerging as an important fungal complication of COVID-19, affecting an average of 3.1% of patients hospitalized with COVID-19, 8.9% of patients admitted to the intensive care unit (ICU), and an average of 20.1% of those requiring invasive ventilation. Diagnosis of CAPA is challenging in patients with COVID-19-associated ARDS, as clinical picture and radiological findings of CAPA resemble those of severe COVID-19, and blood tests lack sensitivity due to the primarily airway invasive growth of *Aspergillus* in non-neutropenic patients. Testing of bronchoalveolar lavage (BAL) with fungal culture, galactomannan (GM), *Aspergillus* polymerase chain reaction (PCR), or the *Aspergillus* GM lateral flow assay (LFA) is therefore preferred, but due to the presumed risk of COVID-19 transmission through bronchoscopies, sampling of the primary infection site is still not performed consistently across ICUs. The high prevalence rates of CAPA in critically ill patients requiring invasive ventilation together with the difficulties in diagnosis and the devastating overall mortality rates of over 50% could justify clinical trials evaluating antifungal prophylaxis in COVID-19 patients with acute respiratory failure. One retrospective single-centre case series from Belgium has reported the successful use of prophylaxis in terms of CAPA case reduction with inhaled liposomal Amphotericin B in a cohort of ICU patients with severe COVID-19; however, studies evaluating systemic antifungal prophylaxis are lacking.

Objective:

Primary: To evaluate the effectiveness of mould-active antifungal prophylaxis in preventing CAPA in critical care patients with COVID-19-associated acute respiratory failure.

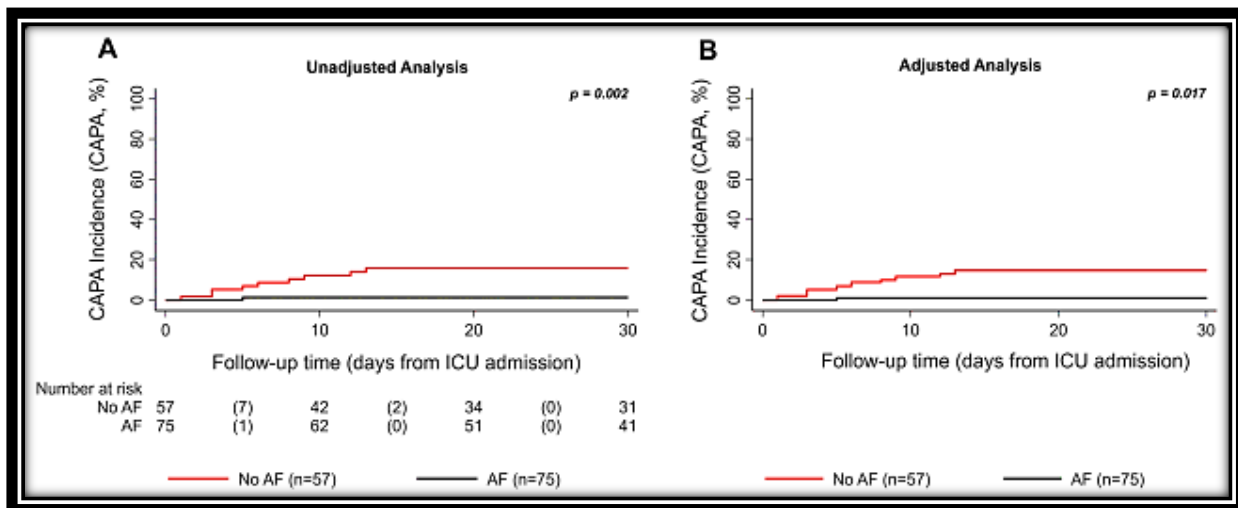
Secondary: The evaluation of a potential survival benefit associated with antifungal prophylaxis as well as the impact of CAPA on overall survival.

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Methods: All consecutive patients admitted to intensive care units with COVID-19-associated ARF were included. Comparison between patients with versus without antifungal prophylaxis with respect to CAPA incidence (primary outcome) and mortality (secondary outcome) was done. Propensity score adjustment was performed to account for any imbalances in baseline characteristics. CAPA cases were classified according to European Confederation of Medical Mycology (ECMM)/International Society of Human and Animal Mycoses (ISHAM) consensus criteria.

Results: Among 132 patients included in the study, about 75 (57%) received antifungal prophylaxis (98% posaconazole). Ten CAPA cases were diagnosed, after a median of 6 days following ICU admission. Of those, 9 CAPA cases were recorded in the non-prophylaxis group and one in the prophylaxis group, respectively.

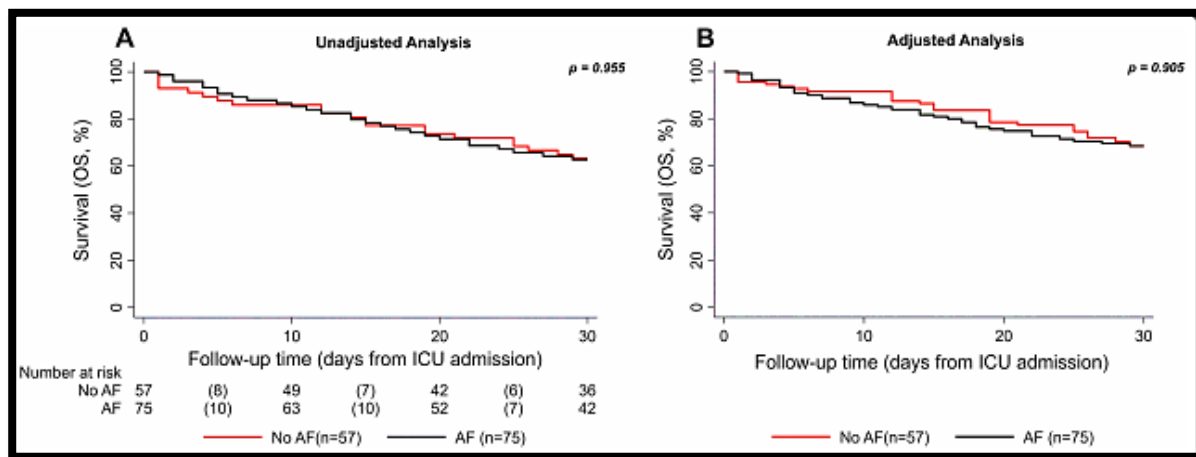
CAPA incidence according to antifungal prophylaxis



However, no difference in 30-day ICU mortality could be observed. Thirty-day CAPA incidence estimates were 1.4% (95% CI 0.2–9.7) in the MAFP group and 17.5% (95% CI 9.6–31.4) in the group without MAFP ($p=0.002$).

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30-day ICU survival according to antifungal prophylaxis



The respective sub distributional hazard ratio (sHR) for CAPA incidence comparing the MAFP versus no MAFP group was of 0.08 (95% CI 0.01–0.63; $p=0.017$).

Conclusion: In ICU patients with COVID-19 ARF, antifungal prophylaxis was associated with significantly reduced CAPA incidence, but this did not translate into improved survival. Randomized controlled trials are warranted to evaluate the efficacy and safety of MAFP with respect to CAPA incidence and clinical outcomes.

Source: Hatzl et al. Antifungal prophylaxis for prevention of COVID-19-associated pulmonary aspergillosis in critically ill patients: an observational study. Crit Care. 2021; 25: 335

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High-flow nasal oxygen cannula vs. noninvasive mechanical ventilation to prevent reintubation in sepsis: a randomized controlled trial

Background

Extubation failure may be a serious clinical event related to a poor outcome in patients that have recovered from respiratory failure. The reported incidence range of reintubation after planned extubation is between 10 and 20%, counting on patient characteristics, weaning modality, and therefore the follow-up period. The risk of death is up to fivefold above in patients who don't experience extubation failure. In addition, reintubated patients experience longer stays within the medical care unit (ICU) and therefore the hospital. Previous studies have assessed measures that would prevent reintubation. Noninvasive mechanical ventilation (NIV) provides intermittent positive pressure with high and adjustable oxygen concentrate airflow and has been proven to decrease the danger of reintubation, especially in hypercapnic patients. Guidelines from the European Respiratory Society and the American Thoracic Society recommend that NIV should be used to prevent reintubation in at-risk patients including patient age > 65 years and those with underlying cardiac or chronic respiratory illness. High-flow nasal oxygen cannula (HFNC) may be a newer modality that gives heated, humidified air with an adjustable oxygen concentration via a wide-bore nasal cannula. A large-scale randomised controlled trial (RCT) comparing HFNC with conventional oxygen therapy after extubation in low-risk patients reported that HFNC was related to a lower rate of reintubation at 72 hrs. A recent RCT in critically ill and post-cardiothoracic surgery patients at high risk of extubation failure, reported that HFNC wasn't inferior to NIV. Moreover, an observational study showed that HFNC was as effective as NIV in preventing reintubation with a lower rate of device intolerance. Despite these encouraging studies, there are not any studies that conclude that either HFNC or NIV is superior to stop reintubation, particularly in recovered sepsis patients. Approximately 80% of sepsis/septic shock patients experience respiratory failure and need mechanical ventilation. The in-hospital mortality of

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those patients ranges from 28% to 51.2%, which is above that in patients without respiratory failure.

Moreover, when patients improve and are extubated, approximately 19% experience extubation failure.

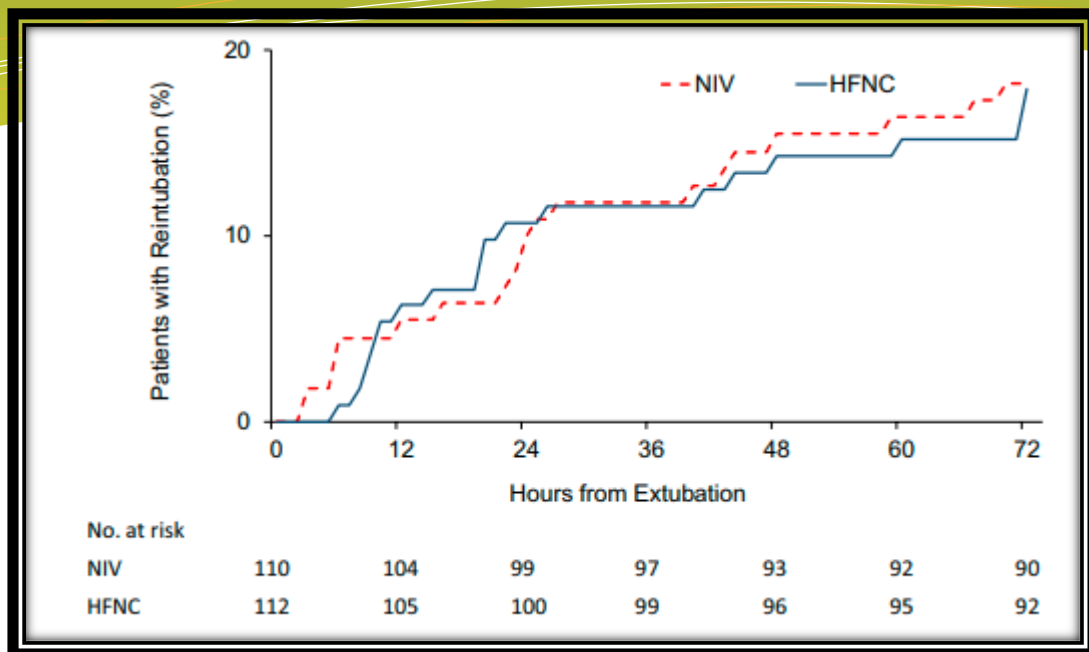
The high proportion of extubation failure among sepsis patients could also be explained by fluid overload following septic shock resuscitation, sepsis related cardio myopathy, and deterioration of kidney function. These may end in extubation failure thanks to weaning induced pulmonary edema. Therefore, we compared HFNC vs. NIV to stop extubation failure among sepsis patients.

Methods: A single-centre, prospective, open-labelled, randomised controlled trial at the medical intensive care unit. Sepsis patients who had been intubated, recovered, and passed the spontaneous breathing trial were enrolled and randomly assigned in a 1:1 ratio to receive either HFNC or NIV support immediately after extubation. The primary outcome was rate of reintubation at 72 h after extubation.

Results: Around 222 patients were enrolled and 112 were assigned to the HFNC group and 110 to the NIV group. Both groups were well matched in baseline characteristics. The median [IQR] age of the HFNC group was 66 [50–77] vs. 65.5 [54–77] years in the NIV group. The most common causes of intubation at admission were shock-related respiratory failure (57.1% vs. 55.5%) and acute hypoxic respiratory failure (34.8% vs. 40.9%) in the HFNC and NIV groups, respectively. The duration of mechanical ventilation before extubation was 5 [3–8] days in the HFNC group vs. 5 [3–9] days in the NIV group.

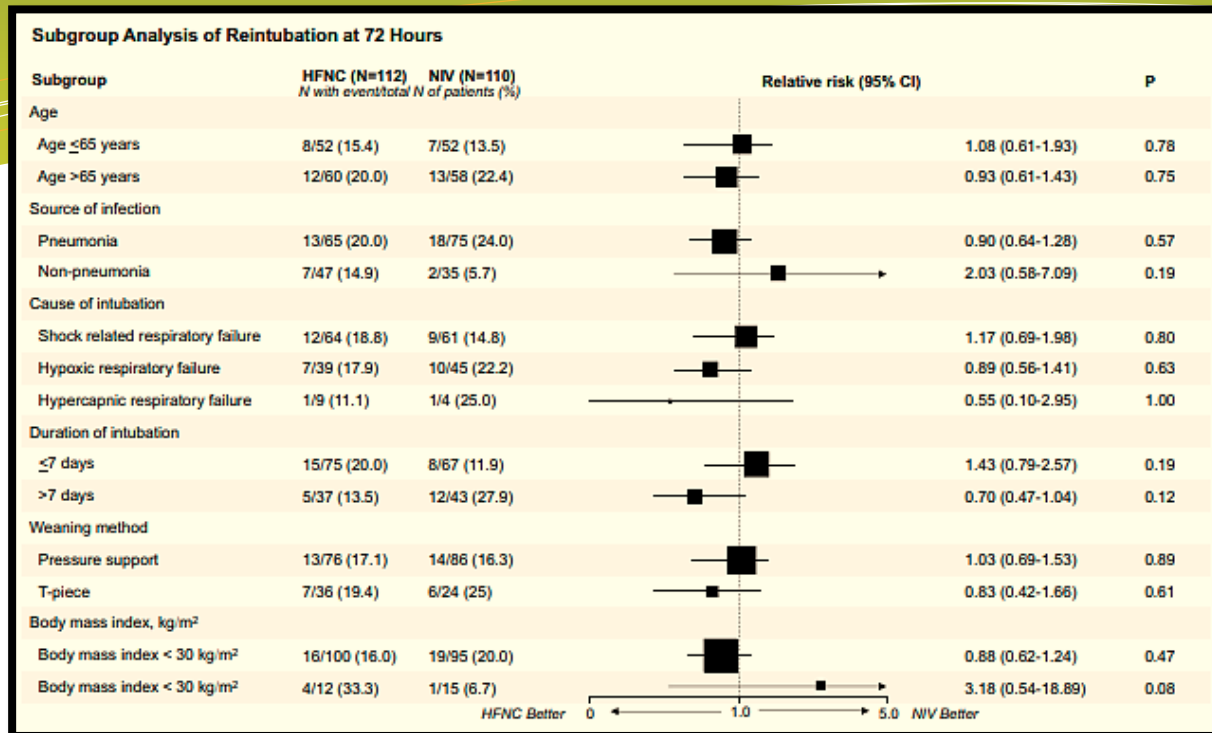
Kaplan–Meier analysis of time from extubation to reintubation

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Risk of reintubation at 72 h after extubation, according to subgroup

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There was no statistically significant difference in the primary outcome: 20/112 (17.9%) in the HFNC group required reintubation at 72 h compared to 20/110 (18.2%) in the NIV group [relative risk (RR) 0.99: 95% confidence interval (CI) (0.70–1.39); P=0.95]. The 28-day mortality was not different: 8/112 (7.1%) with HFNC vs. 10/110 (9.1%) with NIV (RR 0.88: 95% CI (0.57–1.37); P=0.59).

Conclusions: Among sepsis patients, there was no difference between HFNC and NIV in the prevention of reintubation at 72 h after extubation.

Source: Tongyoo et al. Ann. High-flow nasal oxygen cannula vs. noninvasive mechanical ventilation to prevent reintubation in sepsis: a randomized controlled trial. Intensive Care. 2021;11:135

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Introduction

In the last decade, there are quite 40 randomized trials evaluating early mobilization and rehabilitation in medical care units (ICU). Such trials generally aim to scale back the incidence of ICU-acquired weakness (ICUAW) which is related to poor long term survival, physical functioning, and quality of life. At least eight international guidelines have recommended ICU early mobilization and rehabilitation. Despite supporting evidence and guidelines, implementation of ICU mobilization and rehabilitation is very variable.

Create multidisciplinary team

Early mobilization and rehabilitation is more successful in ICUs with a culture that prioritizes and values this intervention. Mobility champions can help develop this culture using leadership and communication skills to teach, train, coordinate, and promote patient mobilization. They support staff with a stress on safety and practical skills to enhance the team's confidence and capabilities.

Use structured quality improvement (QI) processes

A structured QI approach can greatly enhance successful implementation of early mobilization and rehabilitation. One approach to QI includes four steps:

1. Summarizing the evidence
2. Identifying barriers (e.g., sedation or lack of equipment).
3. Establishing performance measures (e.g., sedation targets, frequency, and level of patient mobilization).
4. Ensuring all eligible patients receive the intervention (via appropriate engagement, education, execution, and evaluation).

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Identify barriers and facilitators

A systematic review identified 28 unique barriers to early mobilization and rehabilitation, including patient related barriers (e.g., physiological instability and medical devices), structural barriers (e.g., limited staff and equipment), procedural barriers (e.g., lack of coordination and delayed screening for eligibility), and cultural barriers (e.g., prior staff experience and ICU priorities for patient care). There are many strategies to effectively overcome barriers, including implementation of safety guidelines; use of mobility protocols; inter-professional training, education, and rounds; and inclusion of physician.

Promote multi professional communication

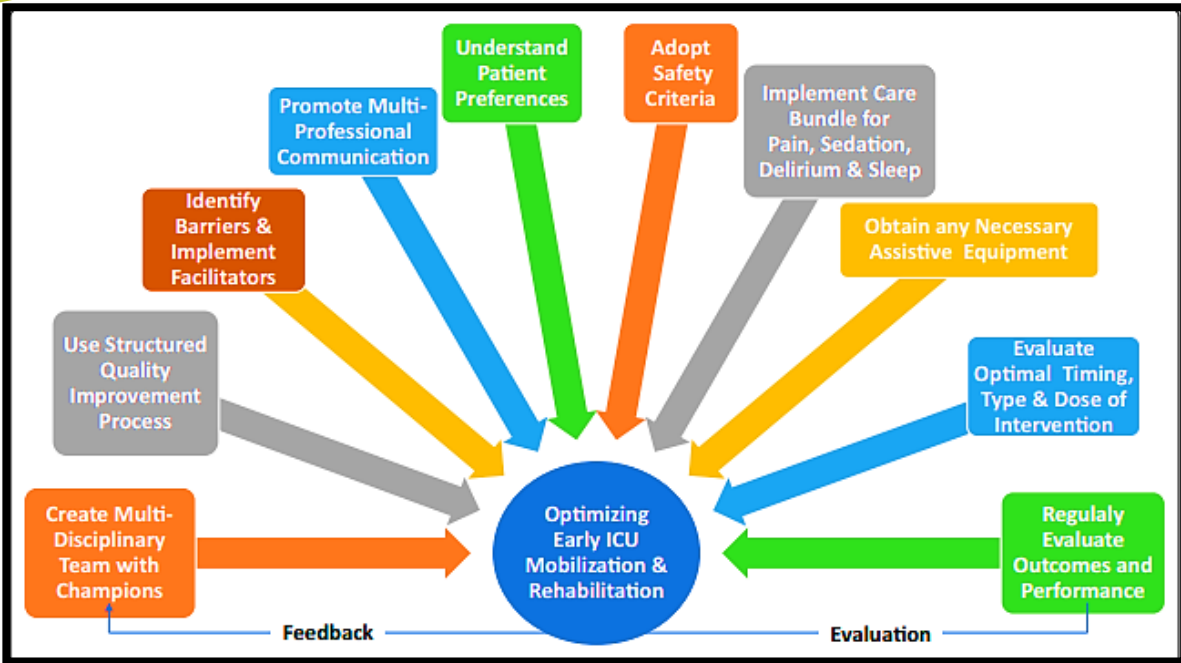
The multi-professional team effort required for early mobilization and program depends on optimal communication. It is recommended that inter-professional communication is facilitated using a structure adapted to the individual ICU that allows (algorithm based) mobilization goals, including an opportunity for all team members to raise concerns and ensure flow of data regarding mobility goals and achievement across staff and over time.

Understand patient preferences

ICU patients' experience with early mobilization and rehabilitation is variable. It may be tiring, uncomfortable and difficult, while at other times be motivating and rewarding for patients. With improving cognitive status, patients could also be shocked by the severity of their muscle weakness. In the early stages of critical illness, patients may like better to specialise in short-time goals (e.g., sitting during a chair) set by the multidisciplinary team. As patients progress, they'll become more engaged in goal setting and longer-term rehabilitation planning (e.g., walking longer distances, sitting outside).

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Ten strategies to optimize early mobilization and rehabilitation in ICU



Adopt safety criteria

Meta-analyses have demonstrated the security of in-bed and out-of-bed ICU mobilization, with rare occurrence of great events. One method of assessing safety may be a traffic signal system that gives specific criteria, across respiratory, hemodynamic, neurological, and other body systems, to be considered in mobilizing individual patients. In this system, “red light” criteria indicate an increased potential for a significant safety event during mobilization requiring experienced decision-making, “yellow light” indicates potential risk that ought to be evaluated in terms of advantages versus risks, and “green light” indicates that mobilization is usually safe.

Implement care bundles for pain, sedation, delirium, and sleep

Patients’ sedation and delirium status may be a common barrier to early mobilization and rehabilitation. More broadly, pain, sedation, delirium, sleep, and early mobilization and rehabilitation are closely inter-related, as considered in clinical guidelines. Assessment and management of those issues, via existing evidence based practices (as synthesized within the guidelines), are important to maximise patients’ ability to participate in rehabilitation.

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Obtain any necessary equipment

Barriers to early mobilization and rehabilitation may include ICUAW, impaired physical functioning, traumatic injuries, and obesity. Equipment can expand treatment options, increase patient mobility and activity levels, and reduce risk of injury to staff. Selecting rehabilitation equipment could also be challenging, with important considerations including the equipment cost/ availability, ability to share equipment between units or patients (including infection control considerations), and therefore the physical space available for patient mobilization and for convenient storage of kit . Evidence supporting use of specific equipment remains evolving, including evaluation of neuromuscular electrical stimulation (NMES), in-bed cycle ergometry, tilt tables, and other devices.

Evaluate optimal timing, type, and dose of intervention

Important knowledge gaps exist regarding exercise, including the timing, type, and dose of interventions. There is some evidence suggesting that starting rehabilitation within 2 or 3 days of ICU admission could also be superior to later initiation. Types of interventions to be considered include active functional mobilization, in bed cycle ergometry, electrical muscle stimulation (with or without passive/active exercises), tilt tables, and use of varied rehabilitation equipment. In addition, the intensity, duration, and frequency of every intervention type are important considerations. Additional research is required to further understand potential benefit or harm. Until that point , clinician judgement will play a crucial role and must be tailored to individual patients and to the dynamic nature of critical illness.

Assess outcomes and performance

Mobility and rehabilitation-related measures, appropriate to the ICU setting and integrated into clinical care, are needed to line patient goals and track their progress, allocate scarce rehabilitation resources to those patients who may benefit the foremost , and conduct evaluations of structured quality improvement programs. Understanding patients' functioning prior to critical illness, and their own goals, are also important considerations.

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Conclusion

Evidence remains evolving about early mobilization in ICU with ongoing large, multi-center trials. Further research is required to know the optimal timing, type and dose of interventions, and their effect on long-term patient outcomes. These 10 strategies provide guidance for implementing early mobilization and rehabilitation within the ICU with the goal of optimizing safety and effectiveness to enhance patients' experiences and outcomes.

Source: Hodgson et al. Ten strategies to optimize early mobilization and rehabilitation in intensive care. Crit Care. 2021;25:324



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