# **Special Article**

# Early Mobilization of Intensive Care Unit ((ICU) Patients

# Konstantinos Koukourikos, RN, MSc, PhDc

Lecturer, Nursing Department, International Hellenic University, Thessaloniki, Greece

## Lambrini Kourkouta, PhD Professor, Nursing Department, International Hellenic University, Thessaloniki, Greece

Christos Iliadis, RN Private Diagnostic Health Center of Thessaloniki, Greece

Vassiliki Diamantidou, MD, MSc in Obstetrics Medicine Internal Medicine Speialist, Intensive Unit Specialist, 251 Airforse Hospital, Athens Greece

Vassiliki Krepia, RN, MSc, PhD General Hospital "Sismanogleion", Athens, Greece

# Areti Tsaloglidou, RN, MSc, PhD Assistant Professor, Nursing Department, International Hellenic University, Thessaloniki, Greece

**Correspondence:** Koukourikos Konstantinos Lecturer, Nursing Department, International Hellenic University, Thessaloniki, Greece. P. O BOX 141. GR - 574 00 Sindos, Thessaloniki GREECE. Email: kokaea@yahoo.gr

#### Abstract

**Introduction:** Early mobilization (active and passive) is an important factor in preventing and treating neuromuscular damage observed in ICU patients mainly due to bed rest and immobilization.

**Purpose:** This is a review regarding the early mobilization of patients in ICU, the role of EMS and is especially referred to the barriers and safety issues arising from the use of mobilization programs.

**Material and methods:** A literature review was performed via valid databases such as Scopus, PubMed, Cinahl for the period 2000-2019 in English language. The following keywords were used: ICUaW, early mobilization, rehabilitation, barriers and safety, loss of muscle mass, immobilization, bed rest.

**Results:** The review shows that mobilization and rehabilitation programs in the early stages of patient care in the ICU can have beneficial effects on patients, bypassing the barriers that may arise and providing safety to patients. The positive elements from their implementation is the continuous improvement of the patients' functionality, the reduction of the dependence on the ventilator and the duration of stay in both the ICU and the hospital.

**Conclusions:** Early mobilization is an important tool for dealing with neuromuscular damage of patients in the ICU and, if it is combined with changes related to the developing culture in the ICU as well as with improvement in the general organization and management of these units, then the future looks bright for hospitalized patients.

**Keywords:** ICUaW, early mobilization, rehabilitation, barriers and safety, loss of muscle mass, immobilization, bed rest.

### Introduction

The operation of the Intensive Care Units in conjunction with better equipment due to the advances of the technology, and the specialized, qualitative care provided to the seriously ill, contributes to the increase of survivors in the ICU (Engel et al., 2013). Although that the restriction, the immobilization, the mechanical support, the use of drugs as well as the prolonged bed rest cause serious physical and psychological damage to the ICU patients, on the other hand they are crucial parts of the provided care (Drolet et al.,2012). It has been observed that, during their hospitalazion and after their discharge from the unit, the patients often exhibit neuromuscular weakness, reduced cognitive functionality and various psychological side effects. These effects lead to main changes in patients' daily life and reduce their quality of life (Herridge et al., 2011) for a long time after their discharge from the hospital (Fan et al., 2014).

Thus, the term Intensive Care acquired Weakness (ICUaW) is now widely accepted and describes the difficult situation experienced by ICU patients. It is a major complication and therefore has attracted the interest of the scientific community. The fact that muscle weakness and nerve damage start from the first days of the patient's hospitalization, means that immediate action needs to be taken as it is considered to be a public health problem (Puthucheary et al., 2013). The prevalence of ICUaW varies and depends mainly on the severity of the disease and the diagnostic technique used. According to a modern review of 33 studies (n = 2686), the probability of occurring ICUaW is estimated at 40% in patients who are on mechanical ventilation for more than 7 days (Appleton, Kinsella, Quasim., 2015) while in another study, under the same conditions, the percentage is raised up to 58% (Griffiths & Hall, 2010).

For ICU patients, the term "early mobilization" (EM) refers to the implementation of a physiotherapy program (passive mobilization, active mobilization and respiratory muscle training) or new mobilization techniques (ergometry cycle, or neuromuscular electrical stimulation) at an early stage of a patients stay at the hospital (less than 5-7 days)(Cameron et al., 2015). While there is a significant interest by the scientific community for the early mobilization programs at ICU patients, the results of 2 studies show that their implementation is not widely used. A 1-day study by Nydahl et al., (2014) across Germany, the aim of which was to determine the rate of early patient mobilization in ICUs, showed that only 24% of all mechanically supported patients and only 8% of patients with endotracheal tube were mobilized in their bed as part of their care. Dealing with modifiable mobilization barriers such as deep sedation, is an important parameter for increasing such programs in German ICUs. A similar study in southern Brazil showed that the frequency of mobilization programs in ICUs was even lower. In only 10% of mechanically supported patients and 2% of patients carrying endotracheal tubes, a

mobilization protocol was used (Fontela et al., 2018a).

Early patient mobilization: One possible treatment option to deal with the muscle mass loss in critically ill ICU patients is their early mobilization. Mobilization is defined as "physical activity that is performed at a suitable intensity, providing physical benefits for the body and helping (affecting) the circulation, central and peripheral perfusion, ventilation (oxygenation) and the level of consciousness". (Castro-Avila et al., 2015). The rehabilitation programs consist of the following therapeutic strategies: passive and active range of motion, active side to side turning, cycling in bed, exercises in bed, sitting on the edge of the bed, transferring from bed to a chair, marching on the spot, ambulation, hoist therapy, tilt table, active resistance exercises, and electrical muscle stimulation. (Amidei, 2012) The start of the mobilization program, as well as the frequency of its implementation are closely related to the expected results (Farhan et al., 2016). The mobilization techniques must be relative to the patient's abilities but also to his level of cooperation. The correct choice of technique requires a detailed examination by health experts, which includes taking the patient's medical history and evaluating the following parameters: cardiac reserve, respiratory reserve, and factors affecting the overall clinical picture of the patient (Truong et al., 2009). The same scientists (Truong et al., 2009) in their study report that staying in bed for extended periods is known to alter fundamental aspects of muscle structure, function and biology. They also point out that mechanical muscle unloading leads to oxidative stress, imbalances in protein synthesis and cell death while at the same time, it seems to be exacerbated by systemic inflammation, infection, hypercortisolemia (overproduction of cortisol) and malnutrition. The same study emphasizes that in both healthy volunteers and critically ill patients, clinostatism is associated with rapid loss of muscle mass and maximal strength.

Other studies (Meyer et al., 2015, Bloch et al., 2015) emphasize the fact that ICU patients due to mechanical ventilation and immobility are at high risk of developing ICUaW, so health professionals should properly evaluate these cases and act quickly implementing individualized programs. It is noted that to patients with muscle atrophy, the changes observed at the cellular and molecular level are

due to a reduction in cell membrane stimulation, and alterations to the link between protein production and degradation resulting in increased protein degradation. They are also due to an increase of the occurrence of free radicals, a reduction of the antioxidant defense with the occurrence of oxidative stress leading to the increase of inflammatory process and the presence of interleukins.

The study of Schweickert et al., (2009) reports significant benefit for the patients in terms of functional capacity due to the early mobilization and rehabilitation upon discharge from hospital. Other studies have also looked at the ability of patients to walk on their way out of the hospital. A common element of the studies is the division into 2 groups, the one that received the immediate intervention and the other one that received the usual care depending on the situation. The results showed that the group that received the immediate intervention walked further, thus increasing its mobility (Hanekom, Louw, Coetzee, 2012; Denehy et al., 2013). In the study of Denehy et al., (2013) related to the quality of patient's life, the population of participants was divided into 2 groups. In both of them poorer quality of life than the average (mean population) was shown, while in the study of Schweickert et al., (2009), the results (in terms of quality of life) were favorable to those who had received intervention (early mobilization).

Regarding the duration of mechanical ventilation, Schweickert et al, (2009) showed that the patients from the intervention group spent fewer days in mechanical ventilation than the control group, while Routsi et al., (2010) reported fewer days of dependence on mechanical ventilation, but this result was not statistically significant in both cases. The study of Ota et al., (2015) on the other hand, showed that the duration of mechanical support was shorter in the intervention group than in the control group and this difference was statistically significant. The study of Moss et al., (2016) in ICU patients who needed mechanical support for at least 4 days, showed that there were no significant differences between the 2 groups (intervention and control) even after their discharge from the hospital. Furthermore, the length of stay in the ICU and the hospital did not differ significantly between the comparison groups in 2 modern studies (Brummel et al., 2014; Arias-Fernandez, 2018).

In the study of Dantas et al., (2012) aiming at evaluating the effectiveness of early mobilization protocol in the respiratory and peripheral muscles of ICU patients (n = 59), it was shown that there were positive differences, but not statistically significant, both in muscle strengthening as well as in staying in mechanical ventilation, in ICU and in the hospital in general.

According to the European Society of ICU Task force of Physiotherapy (Gosselnik et al., 2008) patients' mobilization should be one of the most important goals of physiotherapists. It is an indisputable fact that mobilization contributes to the awakening of the patient, the prevention of thrombophlebitis, muscle atrophy as well as weakness of the respective muscle groups. It also contributes to the treatment of pressure ulcers, the facilitation of vascular circulation, and the treatment of systemic release of the patient from the ventilator.

In the study of Hodgson et al., (2016) aiming at investigating the application of early mobilization in patients with mechanical ventilation, it was shown that this intervention is not only feasible but also safe. It also concluded that early mobilization led to an increase in the duration and level of active exercises. In the study of Bailey et al., (2007) it is supported that mobilization is safe and feasible with minor changes in blood pressure (below 1%), high degree of desaturation or even movement of the feeding tube. This study was consisted of 103 patients and included three exercises in total: seating of the seriously ill person on the edge of the bed, seating in a chair and walking. On the other hand, the study of De Figueiredo et al., (2020) showed that the implementation of mobilization programs on burn patients admitted to ICU, resulted in a low level of mobility during the period of being connected to the ventilator and also a low level of functionality upon their discharge from the hospital.

In a meta-analysis of Hu et al., (2019) it is reported that early mobilization is beneficial in restoring the functionality of ICU patients, leading to the improvement of muscle strength and the ability of patients to walk independently, the reduction of the ICUaW syndrome occurrence and the mortality rate in hospitals.In another meta-analysis of Zang et al., (2020) it is reported that early mobilization was effective in preventing the occurrence of ICUaW, reducing the length of stay in the ICU and in hospital, and improving their mobility. However, there was no reduction in the mortality rate, even in days without the use of a ventilator. Increased functionality of patients admitted to ICU with vascular stroke upon their discharge from the hospital and a better quality of life is also presented in the study of Alamri et al., (2019). The combination of passive and active mobilization programs for patients who are in mechanical ventilation in ICU is a safe process benefits the patients (reducing that the connection time to the ventilator, reducing the time spent in the ICU and improving operational capacity) as long as there is a financial support for such programs and teamwork of various health professionals (Hruska., 2016). Early mobilization of patients with acute respiratory failure (n=153) depended on mechanical ventilation showed that the time of dependence on the ventilator and stay in the ICU had been contribution reduced, and the of the multidisciplinary therapeutic team including patient's family was important (Lai et al., 2017). According to the study of Gomez-Cabrera, Domenech & Vina (2008), the contribution of mobilization to reducing oxidative stress and inflammation is remarkable. During moderate to vigorous exercise (60% to 75% of maximum oxygen intake) in skeletal muscles an increase in the expression of antioxidant enzyme production is seen, thus offering increased protection against oxidative stress.

Furthermore, according to Petersen & Pedersen (2005), moderate exercise leads to an increased production of anti-inflammatory cytokines. Interleukin-6 (IL-6) (which has antiinflammatory properties) is the first cytokine that can usually be increased during exercise, up to 100 times more than the reference values observed before exercise. After the exercise, IL-6 gradually decreases (Febbraio, Pedersen, 2002). Overall, reducing oxidation as well as increasing anti-inflammatory cytokines during moderate exercise can play an important role in maintaining muscle mass to th critically ill patients.

Aerobic exercise is a key component that reduces muscle weakness, increases the time spent off the ventilator and improves the functionality of patients who have been left for a long time under mechanical ventilation. Burtin et al., (2009) implemented a twenty-minute exercise program, five times a week, the results of which showed an increase in their functional exercise capacity, quadriceps force and overall improvement of patient's functionality. In addition, according to the researchers, frequent repetition of lowintensity exercises seems to positively affect muscle mass and functional capacity while also contributing to increased production of oxidative enzymes.

Early mobilization in pediatric ICU (PICU) is gaining momentum, but there are still no major studies related to the functionality and psychological impact of its implementation. The evidence shows that critically ill children mobilization is safe and feasible, but in order to improve the survival of pediatric ICU patients, it is important to minimize sedation, recognize the importance of delirium, and promote early mobilization programs (Walker & Kudchadkar, 2018).

Electrical neuromuscular stimulation: Patients who cannot move and active mobilization cannot be performed to them, passive mobilization through electrical neuromuscular stimulation helps them to avoid muscle mass loss and atrophy. At the same time, its contribution to the avoidance of deformities, pressure ulcers as well as to the improvement of pulmonary ventilation is remarkable. With the right application of early mobilization and the proper evaluation of patients, it seems likely that both respiratory function and the level of consciousness are improved, while muscular atrophy is reduced (Sidiras et al., 2016). The EMS through the application of electricity aims to cause contractions in the muscles as well as activate the skeletal muscles. Thus, muscle exercise can be achieved without the presence of voluntary movement of body parts. When the muscle is stimulated by artificial means, a different activation of muscle units is observed compared to normal voluntary activation. While the electrodes are placed trans dermally above the surface of the muscle, the activation of the muscle is not due to the direct stimulation of the muscle fibers but due to the stimulation of the intramuscular branches of the nerve (if the neural pathway is intact) ( Bouchla et al., 2009). According to Robinson., (2008) the most important factors affecting the strength of muscle contraction are the number of muscle fibers used. This depends on the duration of the stimulus and intensity, as well as on the frequency of stimulation of the peripheral nerve. Low intensity currents, for instance, are not capable of causing muscle contraction. It seems, therefore, that EMS can achieve activation in the large motor units, that cannot be activated during voluntary contraction. (Gregory & Bickel, 2005).

Several studies try to shed light on the role of stimulation neuromuscular electrical in mobilizing ICU patients in both Greek and international hospitals. In a study of Routsi et al., (2010) it is reported that daily EMS (electrical neuromuscular stimulation) sessions prevent the development of polyneuromyopathy (CIPNM) in patients hospitalized in the ICU and also result in a shorter weaning duration. A combination of EMS and exercise regimen on 144 ICU patients over 18 years old who were mechanically supported for at least 3 days, was included in the research framework of Dos Santos et al. (2020) study. This study showed that the above-mentioned method was well tolerated by patients and there was a reduction in the time spent to mechanical ventilation. On the other hand, in a similar study, it was resulted that the effect of EMS and personalized physiotherapy on the muscle strength of 128 ICU patients did not lead to a further improvement in patients muscle strength and functional status on their discharge from the hospital (Patsaki et al., 2017). In another study of Dall' Acqua et al., (2017) ICU patients (n=25) who were on mechanical ventilation (24-48 hours) were divided into 2 groups. In the first one EMS and physiotherapy was applied while in the other group a false EMS and physiotherapy program was used. The aim of the study was to estimate muscle thickness in ICU patients. It was shown that the thickness of the rectal abdominal muscle and thoracic muscle was maintained in the intervention group while there was a decrease in the thickness of the control group. There was also a differentiation in the length of stay between the two groups in the ICU, with a shorter stay in the intervention group. In a systematic review and meta-analysis of Zayed et al. (2020), it was demonstrated that EMS in combination with routine ICU care was not associated with significant variations in muscle strength, ICU mortality, duration of mechanical ventilation or duration of ICU stay compared to standard care provided to hospitalized ICU patients. In the study of Fischer et al., (2016) on a sample of 54 patients who had undergone cardiac surgery, EMS was applied to investigate whether loss of muscle thickness and muscle strength, as well as variation in muscle thickness and strength during the period from

preoperative period to hospital discharge, is prevented. The participants of the study were divided into 2 groups. In the first one, EMS was applied for 14 days while in the second, although electrodes had been placed, no electricity was applied. The results showed that EMS had no effect on muscle thickness, but it was associated with a higher rate of muscle strength recovery during ICU stay. Upon discharge from the hospital, patients had regained preoperative muscle strength levels, but they still appeared residual functionality and reduced muscle thickness compared to pre-ICU levels in both groups.

Barriers to the implementation of early mobilization: Early mobilization (active and passive) is an important measure to prevent complications for patients hospitalized in ICU. However, it is not always possible to implement it because problems and barriers are constantly emerging (Koukourikos, Tsaloglidou & Kourkouta, 2014). Several studies have dealt with this issue, the importance of which is also highlighted by their increasing number. In the study of Goodson et al., (2018) is documented that the members of the multidisciplinary team with a high level of expertise and experience of over 10 years in ICU have a significantly fewer problems in implementing mobilization and rehabilitation programs.

In the systematic review of Dubb et al., (2016) the hemodynamic instability, the presence of vascular and other catheters, sedation and the reduced level of patient consciousness are referred to as barriers. In addition, barriers related to the ICU organization, such as the lack and inadequate training of the staff and the absence of an organized program for the patient's early mobilization, are highlighted. Other problems are related to the culture developed in the ICU, such as the lack of priority in the implementation of such programs, the lack of knowledge and understanding of the benefits, safety and mobilization techniques. Finally, the barriers observed in the process are also important, such as the lack of coordination and communication among health professionals. It is not always clearly defined who is responsible for the selection and integration of patients into the program and there is also ambiguity regarding the responsibilities, the role of each health professional and the objectives set out in the program. Inadequate staff training, lack of understanding of the benefits of early

mobilization, inadequate interdisciplinary communication and lack of leadership in implementing the program, were the main barriers identified by Dafoe et al., (2015). In a study aimed at exploring the knowledge and views of the interdisciplinary team's members working in ICU on the barriers regarding the implementation of mobilization programs, it was found that the main obstacles are considered to be staff shortage, patient repression, delirium, the risk of musculoskeletal injuries and excessive work stress (Fontela, Forgiarini, Friedman, 2018b).

Furthermore, sleepiness, hemodynamic instability, respiratory contraindications and medical objections were the main barriers identified in the study (n=202) of Brock et al. (2018). In the qualitative study of Barber et al. (2015), it is also mentioned that the major barriers to mobilization are the development of a particular culture in ICU, the lack of financial resources, prioritization and leadership.

Safety of early mobilization programs: Given the increase in literature on the subject of ICUaW and its accompanying complications, early mobilization and rehabilitation is now drawing the attention of experts. Despite minor concerns about their implementation, the safety of the programs is becoming key issue and many studies are dealing with it. In the study of Damluji et al. (2013),101 patients who carried a femoral catheter and to whom a mobilization program was implemented (standing - walking, ergometry cycle and exercises in bed) were included. No safety issue was observed and so it can be concluded that the presence of a femur catheter does not preclude patients' mobilization. Adler & Malone (2012) in their study report the presence of adverse events such as line removal or other devices. There were also variations in heart rate, in pulse oximetry and blood pressure. Furthermore, the need of changing medical commands (administration of sedatives; the most common side effect was oxygen des saturation) was obvious. All the above-mentioned side effects are, according to authors, associated with patient safety, but as their occurrence is not frequent (< 2%), it is concluded that mobilization programs are quite safe. Another study analyzed the results of a prototypical mobility protocol, which was launched within 48 hours of mechanical ventilation. None of the 106 patients, who participated in the mobilization program, experienced an accidental removal of any

medical device or any life-threatening condition (Morris et al., 2008)

**Conclusions:** Neuromuscular disorders associated with hospitalization in ICU are increasingly recognized as contributing factors to short- and long-term physical injuries. Bed rest, sedation, drug administration and immobilization are strongly associated with neuromuscular dysfunction and physical injuries, whereas early (active and mobilization passive) and rehabilitation can be a valuable intervention to mitigate these consequences.

## References

- Adler, J., Malone, D. (2012). Early mobilization in the intensive care unit: a systematic review. Cardiopulmonary physical therapy journal, 23(1), 5–13
- Alamri, M. S., Waked, I. S., Amin, F. M., Al-Quliti, K. W., Manzar, M. D. (2019). Effectiveness of an early mobility protocol for stroke patients in Intensive Care Unit. Neurosciences (Riyadh, Saudi Arabia), 24(2), 81–88.
- Amidei, C. (2012). Mobilization in critical care: A concept analysis. Intensive and Critical Care Nursing, 28 (2), 73-81
- Appleton, R, Kinsella, J, Quasim, T. (2015). The incidence of intensive care unit-acquired weakness syndromes: A systematic review. JICS, 16(2), 126-136
- Arias-Fernández, P., Romero-Martin, M., Gómez-Salgado, J., & Fernández-García, D. (2018).
  Rehabilitation and early mobilization in the critical patient: systematic review. Journal of physical therapy science, 30(9), 1193–1201.
- Bailey, P., Thomsen, G. E., Spuhler, V. J., Blair, R., Jewkes, J., Bezdjian, L., Veale, K., Rodriquez, L., & Hopkins, R. O. (2007). Early activity is feasible and safe in respiratory failure patients. Critical care medicine, 35(1), 139–145.
- Barber, E. A., Everard, T., Holland, A. E., Tipping, C., Bradley, S. J., & Hodgson, C. L. (2015). Barriers and facilitators to early mobilisation in Intensive Care: a qualitative study. Australian critical care: official journal of the Confederation of Australian Critical Care Nurses, 28(4), 177–183.
- Bloch, S. A., Lee, J. Y., Syburra, T., Rosendahl, U., Griffiths, M. J., Kemp, P. R., & Polkey, M. I. (2015). Increased expression of GDF-15 may mediate ICU-acquired weakness by downregulating muscle microRNAs. Thorax, 70(3), 219–228.
- Bouchla, A, Karatzanos, E, Gerovasili, V, Zerva, E, Nanas S. (2009). Neuromuscular electrical stimulation as an alternative means of exercise for the critically ill, Archives of Hellenic Medicin , 26(6):759–777
- Brock, C., Marzano, V., Green, M., Wang, J., Neeman,

T., Mitchell, I., & Bissett, B. (2018). Defining new barriers to mobilisation in a highly active intensive care unit - have we found the ceiling? An observational study. Heart & lung: the journal of critical care, 47(4), 380–385.

- Brummel, N. E., Girard, T. D., Ely, E. W., Pandharipande, P. P., Morandi, A., Hughes, C. G., Graves, A. J., Shintani, A., Murphy, E., Work, B., Pun, B. T., Boehm, L., Gill, T. M., Dittus, R. S., & Jackson, J. C. (2014). Feasibility and safety of early combined cognitive and physical therapy for critically ill medical and surgical patients: the Activity and Cognitive Therapy in ICU (ACT-ICU) trial. Intensive care medicine, 40(3), 370– 379.
- Burtin, C., Clerckx, B., Robbeets, C., Ferdinande, P., Langer, D., Troosters, T., Hermans, G., Decramer, M., Gosselink, R. (2009). Early exercise in critically ill patients enhances short-term functional recovery. Critical care medicine, 37(9), 2499–2505.
- Cameron, S, Ball, I, Cepinskas, G, Choong, K, Doherty, TJ, Ellis, CG, et al. (2015). Early mobilization in the critical care unit: A review of adult and pediatric literature. J Crit Care, 30(4), 664-72.
- Castro-Avila, AC, Serón, P, Fan, E, Gaete, M, Mickan, S (2015) Effect of Early Rehabilitation during Intensive Care Unit Stay on Functional Status: Systematic Review and Meta-Analysis. PLoS One, 10(7), e0130722.

https://doi.org/10.1371/journal.pone.0130722

- Dafoe, S, Chapman, MJ, Edwards, S, Stiller, K. (2015). Overcoming barriers to the mobilization of patients in an intensive care unit. Anaesth Intensive Care, 43(6):719-27.
- Dall' Acqua, AM, Sachetti, A, Santos, LJ, Lemos, FA, Bianchi, T, Naue, WS, Dias, AS, Sbruzzi, G, Vieira, SR. (2017). MoVe- ICU Group. Use of neuromuscular electrical stimulation to preserve the thickness of abdominal and chest muscles of critically ill patients: A randomized clinical trial. J Rehabil Med, 49(1) 40-48.
- Damluji, A., Zanni, J. M., Mantheiy, E., Colantuoni, E., Kho, M. E., Needham, D. M. (2013). Safety and feasibility of femoral catheters during physical rehabilitation in the intensive care unit. Journal of critical care, 28(4), 535.e9–535.e5.35E15.
- Dantas, C. M., Silva, P. F., Siqueira, F. H., Pinto, R. M., Matias, S., Maciel, C., Oliveira, M. C., Albuquerque, C. G., Andrade, F. M., Ramos, F. F., & França, E. E. (2012). Influence of early mobilization on respiratory and peripheral muscle strength in critically ill patients. Revista Brasileira de terapia intensiva, 24(2), 173–178.
- De Figueiredo, T. B., Utsunomiya, K. F., de Oliveira, A., Pires-Neto, R. C., & Tanaka, C. (2020). Mobilization practices for patients with burn injury in critical care. Burns: journal of the International Society for Burn Injuries, 46(2),

314-321.

- Denehy, L., Skinner, E. H., Edbrooke, L., Haines, K., Warrillow, S., Hawthorne, G., Gough, K., Hoorn, S. V., Morris, M. E., Berney, S. (2013). Exercise rehabilitation for patients with critical illness: a randomized controlled trial with 12 months of follow-up. Critical care (London, England), 17(4),
- Dos Santos, FV, Cipriano, G, Vieira, L, Güntzel Chiappa, AM, Cipriano, GBF, Vieira, P, Zago, JG, Castilhos, M, da Silva, ML, Chiappa, GR.(2020). Neuromuscular electrical stimulation combined with exercise decreases duration of mechanical ventilation in ICU patients: A randomized controlled trial. Physiother Theory Pract. 36(5), 580-588.
- Drolet, A., DeJuilio, P., Harkless, S., Henricks, S., Waters, C., & Wiliams, S. (2012). Move to improve the feasibility of using an early mobility protocol to increase ambulation in the intensive and intermediate care settings. Physical Therapy Journal, 93(2), 1-11.
- Dubb, R, Nydahl, P, Hermes, C, Schwabbauer, N, Toonstra, A, Parker, AM, Kaltwasser, A, Needham, DM. (2016). Barriers and Strategies for Early Mobilization of Patients in Intensive Care Units. Ann Am Thorac Soc, 13(5), 724-30.
- Engel, H., Needham, D., Morris, P., Gropper, M.(2013). ICU early mobilization: from recommendation to implementation at three medical centers. Crit. Care Med. 41(9 suppl 1) S69–S80. .
- Fan E, Dowdy DW, Colantuoni E, Mendez-Tellez PA, Sevransky JE, Shanholtz C, et al. (2014). Physical complications in acute lung injury survivors: a two-year longitudinal prospective study. Crit Care Med, 42(4), 849–859.
- Farhan, H., Moreno-Duarte, I., Latronico, N., Zafonte, R.,Eikermann, M. (2016). Acquired Muscle Weakness in the Surgical Intensive Care Unit: Nosology, Epidemiology, Diagnosis, and Prevention. Anesthesiology, 124(1), 207–234
- Febbraio, M. A.,Pedersen, B. K. (2002). Musclederived interleukin-6: mechanisms for activation and possible biological roles. FASEB journal: official publication of the Federation of American Societies for Experimental Biology, 16(11), 1335– 1347.
- Fischer, A., Spiegl, M., Altmann, K., Winkler, A., Salamon, A., Themessl-Huber, M., Mouhieddine, M., Strasser, E. M., Schiferer, A., Paternostro-Sluga, T., & Hiesmayr, M. (2016). Muscle mass, strength and functional outcomes in critically ill patients after cardiothoracic surgery: does neuromuscular electrical stimulation help? The Catastim 2 randomized controlled trial. Critical care (London, England), 20, 30.
- Fontela, P., Lisboa, T., Forgiarini-Júnior, L., Friedman, G. (2018)a. Early mobilization practices of mechanically ventilated patients: a 1day point-prevalence study in southern Brazil.

Clinics, 73, e241 doi:10.6061/clinics/2018/e241

- Fontela, P. C., Forgiarini, L. A., Jr, Friedman, G. (2018)b. Clinical attitudes and perceived barriers to early mobilization of critically ill patients in adult intensive care units, 30(2), 187–194.
- Gomez-Cabrera, M.C., Domenech, E., Viña, J. (2008). Moderate exercise is an antioxidant: Upregulation of antioxidant genes by training. Free Radical Biology and Medicine, 44(2), 126–131.
- Goodson, C. M., Friedman, L. A., Mantheiy, E., Heckle, K., Lavezza, A., Toonstra, A., Parker, A. M., Seltzer, J., Velaetis, M., Glover, M., Outten, C., Schwartz, K., Jones, A., Coggins, S., Hoyer, E. H., Chan, K. S., Needham, D. M. (2018). Perceived barriers to mobility in a medical ICU: The Patient Mobilization Attitudes & Beliefs Survey for the ICU. Journal of Intensive Care Medicine. Advance online publication. 18:885066618807120https://doi.org/10.1177/0885 066618807120
- Gosselink, R., Bott, J., Johnson, M., Dean, E., Nava, S., Norrenberg, M., Schönhofer, B., Stiller, K., van de Leur, H., & Vincent, J. L. (2008). Physiotherapy for adult patients with critical illness: recommendations of the European Respiratory Society and European Society of Intensive Care Medicine Task Force on Physiotherapy for Critically Ill Patients. Intensive care medicine, 34(7), 1188–1199.
- Gregory, C. M., & Bickel, C. S. (2005). Recruitment patterns in human skeletal muscle during electrical stimulation. Physical therapy, 85(4), 358–364.
- Griffiths, R., Hall, J. (2010). Intensive care unitedacquired weakness. Critical Care Medicine, 38(3), 779-787.
- Hanekom, S. D., Louw, Q., & Coetzee, A. (2012). The way in which a physiotherapy service is structured can improve patient outcome from a surgical intensive care: a controlled clinical trial. Critical care (London, England), 16(6), R230. https://doi.org/10.1186/cc11894
- Herridge, MS, Tansey, CM, Matte, A, Tomlinson G, Diaz-Granados, N, Cooper, A., et al. (2011).
  Functional disability 5 years after acute respiratory distress syndrome. N Engl J Med, 364(14), 1293– 1304
- Hodgson, C. L., Bailey, M., Bellomo, R., Berney, S.,
  Buhr, H., Denehy, L. ... Webb, S. (2016). A
  Binational Multicenter Pilot Feasibility
  Randomized Controlled Trial of Early Goal-Directed Mobilization in the ICU. Critical Care
  Medicine, 44(6), 1145–1152.
- Hruska, P. (2016). Early Mobilization of Mechanically Ventilated Patients. Critical Care Nursing Clinics of North America, 28(4), 413– 424.
- Hu Y, Hu X, Xiao J, Li D. (2019). Effect of early mobilization on the physical function of patients in intensive care unit: a Meta-analysis. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue, 31(4), 458-463.

- Koukourikos, K., Tsaloglidou, A., Kourkouta, L. (2014). Muscle atrophy in intensive care unit patients. Acta informatica medica: AIM: journal of the Society for Medical Informatics of Bosnia & Herzegovina, 22(6), 406–410.
- Lai, C.C., Chou, W., Chan, K.S., Cheng, K.C., Yuan, K.S., Chao, C.M., Chen, C.M. (2017). Early Mobilization Reduces Duration of Mechanical Ventilation and Intensive Care Unit Stay in Patients with Acute Respiratory Failure. Archives of Physical Medicine and Rehabilitation, 98(5), 931–939.
- Meyer, S. U., Thirion, C., Polesskaya, A., Bauersachs, S., Kaiser, S., Krause, S., & Pfaffl, M. W. (2015). TNF- $\alpha$  and IGF1 modify the microRNA signature in skeletal muscle cell differentiation. Cell communication and signaling : CCS, 13, 4. https://doi.org/10.1186/s12964-015-0083-0
- Morris, P. E., Goad, A., Thompson, C., Taylor, K., Harry, B., Passmore, L., Ross, A., Anderson, L., Baker, S., Sanchez, M., Penley, L., Howard, A., Dixon, L., Leach, S., Small, R., Hite, R. D., & Haponik, E. (2008). Early intensive care unit mobility therapy in the treatment of acute respiratory failure. Critical care medicine, 36(8), 2238–2243.
- Moss, M., Nordon-Craft, A., Malone, D., Van Pelt, D., Frankel, S. K., Warner, M. L., Kriekels, W., McNulty, M., Fairclough, D. L., & Schenkman, M. (2016). A Randomized Trial of an Intensive Physical Therapy Program for Patients with Acute Respiratory Failure. American journal of respiratory and critical care medicine, 193(10), 1101–1110.
- Nydahl, P, Ruhl, AP, Bartoszek, G, Dubb, R, Filipovic, S, Flohr, HJ, et al. (2014). Early mobilization of mechanically ventilated patients: a 1-day point-prevalence study in Germany. Crit Care Med, 42(5), 1178-86.
- Ota, H., Kawai, H., Sato, M., Ito, K., Fujishima, S., Suzuki, H. (2015). Effect of early mobilization on discharge disposition of mechanically ventilated patients. Journal of physical therapy science, 27(3), 859–864.
- Patsaki, I., Gerovasili, V., Sidiras, G., Karatzanos, E., Mitsiou, G., Papadopoulos, E., Christakou, A., Routsi, C., Kotanidou, A., & Nanas, S. (2017).
  Effect of neuromuscular stimulation and individualized rehabilitation on muscle strength in Intensive Care Unit survivors: A randomized trial. Journal of critical care, 40, 76–82.
- Petersen, A. M., & Pedersen, B. K. (2005). The antiinflammatory effect of exercise. Journal of applied physiology (Bethesda, Md.: 1985), 98(4), 1154– 1162.

https://doi.org/10.1152/japplphysiol.00164.2004

Puthucheary ZA, Rawal J, McPhail M, Connolly B, Ratnayake G, Chan P et al.(2013). Acute skeletal muscle wasting in critical illness. JAMA, 310 (15), 1591-600.

- Robinson A. (2008) Physiology of muscle and nerve.
  In: Robinson A, Snyder-Mackler L (eds) Clinical electrophysiology. 3rd ed. Lippincott Williams & Wilkins, Philadelphia, 71–106
- Routsi, C., Gerovasili, V., Vasileiadis, I., Karatzanos, E., Pitsolis, T., Tripodaki, E., Markaki, V., Zervakis, D., Nanas, S. (2010). Electrical muscle stimulation prevents critical illness polyneuromyopathy: a randomized parallel intervention trial. Critical care (London, England), 14(2), R74. https://doi.org/10.1186/cc8987
- Schweickert, W. D., Pohlman, M. C., Pohlman, A. S., Nigos, C., Pawlik, A. J., Esbrook, C. L., Spears, L., Miller, M., Franczyk, M., Deprizio, D., Schmidt, G. A., Bowman, A., Barr, R., McCallister, K. E., Hall, J. B., Kress, J. P. (2009). Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. Lancet (London, England), 373(9678), 1874–1882.
- Sidiras, G, Gerovasili, V, Patsaki, I, Routsi, C, Strantzalis, G, Nanas,S.(2016). Intensive care unit acquired weakness. Archives of Hellenic Medicine,33(2), 151-164 (in Greek)

- Truong, A. D., Fan, E., Brower, R. G., Needham, D. M. (2009). Bench-to-bedside review: mobilizing patients in the intensive care unit--from pathophysiology to clinical trials. Critical care (London, England), 13(4), 216. https://doi.org/10.1186/cc7885
- Walker, T. C., Kudchadkar, S. R. (2018). Early mobilization in the pediatric intensive care unit. Translational pediatrics, 7(4), 308–313.
- Zang, K., Chen, B., Wang, M., Chen, D., Hui, L., Guo, S., Ji, T., Shang, F. (2020). The effect of early mobilization in critically ill patients: A metaanalysis. Nursing in critical care, 25(6), 360–367.
- Zayed, Y., Kheiri, B., Barbarawi, M., Chahine, A., Rashdan, L., Chintalapati, S., Bachuwa, G., & Al-Sanouri, I. (2020). Effects of neuromuscular electrical stimulation in critically ill patients: A systematic review and meta-analysis of randomised controlled trials. Australian critical care: official journal of the Confederation of Australian Critical Care Nurses, 33(2), 203–210.