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Original Research Article

A Prospective Randomised Control Study to Check Best Time to Start Pulmonary Rehabilitation in Intensive Care Unit at a Tertiary Referral Centre

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Abstract:

Background: PICS is considered as a public health burden because of the accompanying neuro-psychological and functional disabilities. Cognitive impairment is reported anywhere between 25% to three-fourth of the of critical care survivors. Major risk factors associated with cognitive impairment are stroke, acute respiratory distress syndrome,sepsis, trauma, respiratory failure necessitating prolonged ventilator support, or premorbid systemic conditions. However, recently, numerous researchers have recommended initiating an early pulmonary rehabilitation, during the period of hospitalization or soon after discharge.An early pulmonary rehabilitation commenced within three weeks after hospitalization is viable, safe, and efficient. It also improves exercise tolerance, reduces symptoms, and augments quality of life.

Objective: To oversee whether with a timely pulmonary rehabilitation patient may be weaned early and discharged from ICU.

Methodology: The present randomized controlled trail was conducted by the at Intensive Care unit of Rashid Hospital which is attached to Rashid University from June 2019 to December 2019. This study consecutively enrolled newly admitted adult patients (≥ 18 years old) who were admitted to ICU, Rashid Hospital, to receive mechanical ventilatory support either noninvasive ventilation (NIV) or invasive mechanical ventilation (IMV) on the day of study inception. A total of 62 patients were included in the study who were further randomized into 36 subjects in H0 is the cohort like the existing one and 26 subjects in H1 which is the cohortwhere the plan to start the timed intervention.

Results: A total of 23 patients were females accounting for 37% of the patients and the remaining 39 were men accounting for 63% of thepatients enrolled in the study. Among the study participants, 44 of them presented with comorbidities accounting for 71% and 18 patients did not report comorbidities, accounting for 29%. Highest number of pulmonary rehabilitations was started on the second day of admission to the ICU. Eleven patients out of the 62 study participants expired in the ICU. Hence, the survival rate was estimated as 82% among the study participants post treatment. No significant difference was seen for weaning days.

Conclusion: Although conclusive evidence could not be generated from the study about the association of early rehabilitation with weaning a gap in research till date has been identified. The research shows that early weaning can be attained irrespective of tailored rehabilitation program, in contrary to certain studies which state that early intervention with a pulmonary rehabilitation aid in early weaning.

Keywords: Rehabilitation, Pulmonary, Weaning, Intensive Care Unit.

Introduction

Mechanical ventilation plays a crucial role in the management of intensive care unit (ICU) patients. Generally, the subjects on a ventilator are considered critical. In such cases the risk of nosocomial infections, particularly pulmonary infections caused because of intubation,is exceptionally high.

The frequency of morbidity and mortality in such cases can reach up to 50 to 70% .[1,2]Alternatively, catheters penetrating the body, remote or wearable patient monitoring apparatus, and underlying systemic health problems, increases incidence and susceptibility to infection. After 24 hours of ventilator assistance pulmonary infections starts arising which are the directcomplications of such appliances. About 20% of patients on mechanical ventilation are prone to such complications.

Artificial mechanical ventilation can be called a “doubtful” advantage. Though a vital necessity to regulate oxygen concentration in patients it may easily lead to an iatrogenic lung damage. Hence it may cause unfavourable damages to the organs apart from the lung. [3] Such harmful impairments, physically and cognitively, experienced by the survivors pose acute impediments after the hospital discharge and affect transition into a home setting to resume a normal life. [4]

Post-discharge complications such as neuromuscular weakness and neuropsychiatric complications can persist anywhere for 5 to 15 years.[4] post-intensive care syndrome (PICS) is new or deteriorating damage in physical, cognitive, or mental health as result of critical illness which persists even after discharge from ICU. It is a condition where a disability remainsin the survivors of critical diseases.[4]

PICS is considered as a public health burden because of the accompanying neuro-psychologicaland functional disabilities. Cognitive impairment is reported anywhere between 25% to three- fourth of the of critical care survivors. Major risk factors associated with cognitive impairmentare stroke, acute respiratory distress syndrome, sepsis, trauma, respiratory failure necessitatingprolonged ventilator support, or premorbid systemic conditions. [5,6]

The risks associated with ICU stay may be negated with early weaning of life support and effective pulmonary rehabilitation. Pulmonary rehabilitation (PR) is defined by the official American Thoracic Society/ European Respiratory Society statement as a “comprehensive intervention based on a thorough patient assessment followed by patient-tailored therapies thatinclude, but are not limited to exercise training, education, and behaviour change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviours” .[7]

Pulmonary rehabilitation involves implementation of controlled physical movements, effective instructions, care and encouragement, and behavioural modification to enhance quality of life post discharge. Pulmonary rehabilitation is a planned schedule intended for ICU survivors withchronic illness to progress lung function and decrease acuteness of symptoms. Its prime objective is to empower patients to attain and preserve their highest amount of independence with lifestyle and bodily function. Pulmonary rehabilitation programs are generally directed towards patients with chronic obstructive lung disorders undertaking lung volume reduction surgery. It might also benefit patients with other serious conditions such as asthma, bronchiectasis, COVID-19, cystic fibrosis, severe lung disease recommended for lung volume reduction surgery, lung cancer patients recommended for lung resection, neuromuscular disorders, pulmonary hypertension, and sarcoidosis. [8]

The optimum period to initiate pulmonary rehabilitation in order to attain highest effectivenessis undetermined, and this indecision raises a significant challenge for the medical practitioners. Clinical strategies endorse delaying by a minimum of three to four weeks following a hospitaldischarge before commencing pulmonary rehabilitation. However, recently, numerous researchers have recommended initiating an early pulmonary rehabilitation, during the periodof hospitalization or soon after discharge. An early pulmonary rehabilitation commenced within three weeks after hospitalization is viable, safe, and efficient. It also improves exercisetolerance, reduces symptoms, and augments quality of life.[6,7,8]

Hence, a randomized interventional study was designed to start early mobilization and chest physiotherapy early (within 24-72 hours) or late (5-7 days) of admission to the critical care unit.

The study was directed to observe the effect of early mobilization on functional improvement in mechanically ventilated patients leading to early weaning.

Objective

To oversee whether with a timely pulmonary rehabilitation patient may be weaned earlyand discharged from ICU.

Methodology

The present randomized controlled trail was conducted at Intensive Care unit of Rashid Hospital which is attached to Rashid University from June 2019 to December 2019.

This study consecutively enrolled newly admitted adult patients (≥ 18 years old) who were admitted to ICU, Rashid Hospital, to receive mechanical ventilatory support either non- invasive ventilation (NIV) or invasive mechanical ventilation (IMV) on the day of study inception. A total of 62 patients were included in the study who were further randomized into 36 subjects in H0 is the cohort like the existing one and 26 subjects in H1 which is the cohort where the plan to start the timed intervention.

Inclusion criteria

- Mechanically ventilated patients
- 18– 90 age group
- Intubated
- Low ventilatory (FIO2 < 50%) and low inotropic support (NA < 0.5mcg/kg/min)
- Start within 72 hours if for early intervention or within 7 days if for late intervention.

Exclusion criteria

- High fraction of inspired oxygen (FiO2) and positive end-expiratory pressure(PEEP)
- High inotropic support
- Multi-organ failure
- Major surgery
- Increased intracranial pressure/ glaucoma.
- Orthopaedic patient with external fixators
- Open abdomen and abdominal surgery in the past one week
  The following is a list of interventions that was included as part of Pulmonary rehabilitation, on ICU admission.
- 45 degrees head up position.
- To keep Ramsay sedation score 3-4 (patient responds to verbal commands or tactilestimuli, but not overly sedated nor agitated)
- Active physiotherapy
- Passive physiotherapy
- Chest physiotherapy

Since the intensivists are rotated regularly, not all patients will receive the intervention. Its onlyon the days that the physician is at work, the interventions can be done. So, the study plannedto compare the weaning durations of patients receiving the interventions. The study hoped to see a positive early weaning and discharge of the patients receiving the intervention. All study participants or the accompanying family members were informed in detailed regarding the characteristics of the study and written consent was obtained. Patients who met the inclusion criteria were enrolled. Initial data was collected by an independent assessor to prevent selection and enrolment bias. Detailed history of the enrolled patients was recorded which included medical record number, age, sex, date of admission to ICU, primary diagnosis,comorbidities, glycemic control, sepsis-multiple organ failure, use of other medications, nutritional status: if under Percutaneous Endoscopic Gastrostomy (PEG), Naso-Gastric Tube Feeding (NGF), Orogastric tube (OGF), or Total Parenteral Nutrition (TPN), mobility status: mobile or immobile, bedbound, restricted, active, or wheelchair assisted. The nature of patient- specific pulmonary rehabilitation methods administered such as Passive Range of Motion (PROM), Active Range of Motion (AROM), and chest physiotherapy (CPT) were recorded. The physiotherapy start date was recorded and tracheostomy status if present or not was reported. Start and stop date of mechanical ventilation and the number of days the patient wason ventilator support was recorded. The number of days the patient was in ICU post physiotherapy and the final discharge date was reported.

Pulmonary rehabilitation was performed by an independent physiotherapist to prevent performance bias. The physiotherapy was started between 0-48 hours for early cohort and after 5 days of ICU admission for the late cohort. As and when the patients were referred for physiotherapy an initial physical assessment was performed.

Conditions or contraindications if any which might further worsen the patient condition was assessed thoroughly before the implementation of pulmonary rehabilitation.

According to patients existing condition at the time of referral a tailored rehabilitation program was designed for each patient. Based on the Glasgow Coma Scale (GCS) if the score was low a passive range of motion (PROM) therapy was tailored and administered. If the GCS was 15/15, an active range of motion (AROM) therapy was tailored and administered. Chest physiotherapy (CPT) was administered to all patients.

All study participants were administered the similar rehabilitation program conducted by a qualified physiotherapist, five sittings every week throughout the intensive care stay.

The consistent training session involved breathing exercise in semi-reclining posture (≥45°), ensuedby cough exercising with repetition set; chest movement isometrics, comprising manual technique and arm elevation with repetition set; strengthening workout for respirational, core,and limbs, comprising antigravity elevation with repetition set; range-of-motion exercises of upper and lower extremities with repetition sets; functional activity training with few repetitions; and endurance training for 5 min. Each session lasted as per the tolerance ability of the patients.

Patient outcomes were considered after extubation, discharge from MICU, or death. Patients were reflected as survived when discharged from the hospital effectively after the said treatment protocols were complete. All data were collected by an independent data assessor apart from the medical fraternities who performed interventions and physiotherapy on the enrolled patients to prevent reporting bias.

Results

All the data were recorded by independent assessors and tabulated to analyze the effect ofpulmonary rehabilitation leading to earning weaning on ICU patients.

Table 1: Demographic Profile of the study subjects

Demographic Profile		Frequency	Percentage
Age group	20-29	5	8%
	30-39	16	26%
	40-49	6	10%
	50-59	7	11%
	60-69	7	11%
	70-79	13	21%
	80-89	5	8%
	90-99	3	5%
Gender	Male	39	63%
	Female	23	37%
Co-Morbidity	Present	44	71%
	Absent	18	29%

A total of 23 patients were females accounting for 37% of the patients and the remaining 39 were men accounting for 63% of the patients enrolled in the study. Among the study participants, 44 of them presented with comorbidities accounting for 71% and 18 patients did not report comorbidities, accounting for 29% [Table 1]. Among the study participants, 40 of them presented showed good Glycemic control accounting for 64% and 22 patients showed poor Glycemic control, accounting for 35%. In the study, sepsis and multiple organ failure was presented in 58% of the study population. Among the study participants, 63% patients were mobile, 5% were bound to wheelchair, 2% was poorly mobile, 3% were restricted, 21% were bedbound, and 6% were immobile [Table 2]. The study participants were divided into different groups to receive pulmonary rehabilitation, namely PROM, AROM, and CPT.

All 62 participants received CPT since the beginning of mechanical ventilation. Out of the 62 participants, 42 patients additionally received PROM and the remaining 18 received AROM based on the clinical conditions.

The study participants were observed for onset of pulmonary rehabilitation. Among the study participants, 65% patients received an early onset pulmonary rehabilitation and 35%received a late onset pulmonary rehabilitation. In the study majority of subjects was started on pulmonary rehabilitations on Day 2 afteradmission (27.4%), 12.9% on Day 1, 9.6% on Day 4, Day respectively, 8.1% on Day 3, 6.4% on Same day, 8th day, 4.8% of day 6, 3.2% on Day 7, Day 9 and day 13 respectively, 1.6% on Day 10, day 11 and day 14 respectively. Twelve patients were on mechanical ventilation for 3 days, followed by 10 patients for 2 days,2 patients for one day and 24 days each, 5 patients each for six and seven days, 3 patients for 8 days, 2 patients for 9 days, and 4 patients each for four and five days. One patient each was reported for 10 days, 11 days, 12 days, 13 days, 15 days, 19 days, 30 days, and 62 days. Five patients were off mechanical ventilation immediately after pulmonary rehabilitation.

Table 2: Distribution of study subjects based on condition of the subjects in the ICU

		Frequency	Percentage
Glycaemic control	Good	40	65%
	Poor	22	35%
Sepsis and Multi organ failure	Yes	36	58%
	No	26	42%
Nutrition and Feeding Methods	Nasogastric tube (NGF)	50	81%
	Percutaneous endoscopicgastrostomy (PEG)	6	10%
	Total Parenteral nutrition (TPN)	5	8%
	Orogastric tube (OGF)	1	1%
Mobility Status	Mobile	39	63%
	Immobile	4	6%
	Wheelchair	3	5%
	Bed Bound	13	21%
	Restricted	2	3%
	Poorly Mobile	1	2%
Tracheostomy	Yes	39	63%
	No	23	37%

Out of 62 patients examined, three patients were off ICU immediately after pulmonary rehabilitation. Two patients each stayed for one day, two days period, and 24 days period. Seven patients each stayed for 3 days and 4 days respectively.

Six patients each stayed for five days and eight days period. Four patients stayed for six days, five patients stayed for seven days, and three patients each stayed for 10 days and 21 days period. One patien each stayed for nine days, 11 days,12 days, 13 days, 14 days, 15 days, 16 days, 17 days, 26 days, 28 days, 62 days, and 70 days respectively. Eleven patients (8%) out of the 62 study participants expired in the ICU. Hence, the survival rate was estimated as 82% among the study participants post treatment.

Table 3: Weaning days comparison between early and late rehabilitation

	N	Mean± SD	Median(IQR)	Range (Min-Max)	P- value
Early Pulmonary Rehabilitation	36	4.94±5.66	3(2,6)	1 to 30	0.743
Late Pulmonary Rehabilitation	24	6.88±12.71	3(1.5,5.5)	0 to 62	

Mann- Whitney Test

Mean weaning days in subjects who received Early Pulmonary Rehabilitation was 4.94±5.66 days and among subjects who received Late Pulmonary Rehabilitation was 6.88±12.71 days. There was no significant difference in Weaning days between two groups.

Discussion

The study was designed with an objective to evaluate the effect of pulmonary rehabilitation, starting late or early, on weaning period in mechanically ventilated patientsin intensive care units. Different methods of pulmonary rehabilitation tailored for specificpatients were administered and the outcome was registered. The pathophysiology triggering weaning failure is intricate, and the comparative significance of the various aspects concerned is not entirely comprehended.

Effect of patient gender on weaning

Numerous analyses have also revealed that men represent over half the patients obtaining mechanical ventilation in the intensive care unit in the study done by Higashijima, et al [9] andKrieger et al.[10]. Nevertheless, there were limited research on the result of gender on scientific outcomes on mechanical ventilation, and the conclusions were inconsistent. Another study used a multivariate analysis to prove that women undergoing mechanical ventilation were at a higher risk for hospital death compared to men in the study done by Meyer et al [11]. In contrast, two other prospective studies done by Al Saif et al [12] and YangK et al [13] showed that gender was not in dependently associated with hospital mortality.

Effect of patient age on weaning

Aging is related with an advancing reduction in lung function. Functional modifications occur in parenchyma and chest wall which reduced static elastic recoil, chest wall conformity, and respiratory muscle potency which may lead to variations in respiratory performance in the study done by Tanaka et al. [14].

One of the studies done by Corbelliniet et al [15] reported that aging effects weaning conditions without producing a surge in weaning failure. Another study done by Verceles et al [16] reported that weaning became difficult withevery five-year increase in age. In our study out of the total 62 study participants, 28 patients were above the age of 60 years and the age did not show any direct correlation to the status of weaning among the participants.

Effect of comorbidities on weaning

Chronic critically ill patients frequently display acute disease conditions, several comorbidities, extended hospitalizations, and recurrent admissions to critical care units. Such incidences are related with poor results and high death rates in the study done by Safdar & Bradley et al [17] and Scheinhorn et al [18]. A study based on their research concluded thathigher comorbidity burden was related to an increase in risk of transfer to critical care. However, additional investigations were required to elucidate the relationship further. In ourstudy comorbidities was present in 71% of the study population. However, the presence of comorbidities did not show any direct correlation with the weaning status of the participants.

Effect of glycemic control on weaning

Hyperglycemia is known to cause deleterious effects on respiratory muscle functions in patients under critical care in the study done by Greet et al. [19]. Studies state that 25% of all mechanically ventilated patients have trouble weaning off in the study done by D. Martin et al [20]. However, the precise proportion of patients with poor glycemic control on mechanical ventilation is uncertain. The data is insufficient on the correlation between diaphragmatic weakness, poor glycemic control, and delayed extubation. Medical research has confirmed that stringent glucose control measures lower the incidence of ICU acquired diaphragm weakness and reduces the period of mechanical ventilation and stay in ICU in the study done by

Calla han & Supinski et al . [21]

Effect of sepsis and multiple organ failure on weaning

Sepsis is among the commonest reasons for hospital mortality worldwide. It continues to be a risk aspect in spite of advanced supportive rehabilitations and medications.

Mechanical ventilation is a critical aid to acutely ill patients including those with sepsis. Therefore, weaning from ventilator is also a top priority. Few patients having sepsis requiremechanical ventilation because of respiratory distress or other non-respiratory organ systems issues. [22,23]

Nutrition status on weaning

Improvement in nutritional status results in improved pulmonary function and makes weaning from mechanical ventilation effortless. Early calculation of nutritional requirementscan aid in recognizing patients requiring nutritional interventions. Enteral nutrition is a preferred in mechanically ventilated patients due to their inability to ingest food orally. Enteral nutrition, a supportive therapy, supplements for both energy and protein necessitiesin the critical care unit. Early enteral nutrition reduces complications, lessens hospital stay, and enhances prognosis. Nutritional support is exclusive for every individual on mechanical ventilation and must be customized to the patient's inherent disease condition as per the study done by Allen & Hoffman et al. [24] In our study, 81% were on nasogastric tube (NGF), 10% patients were on percutaneous endoscopic gastrostomy (PEG), 8% on total parenteral nutrition (TPN), and 1% were orogastric tube (OGF). No direct correlation was established between the nutrition status on early weaning.

Prior mobility status on weaning

Among the study participants, 63% patients were mobile, 5% were bound to wheelchair, 2% was poorly mobile, 3% were restricted, 21% were bedbound, and 6% were immobile. Mechanically ventilated individuals are prone to muscle weakness post admission into critical care set up. Recent outcomes propose early mobilization of such patients might be anefficient intervention in bettering the results in the study done by Clarissa et al. [25]

Tracheostomy status on weaning

Tracheostomy is regularly recommended for patients who are ventilator dependent or are complicated to wean. Even though the benefits of tracheostomy on weaning continue to bedebated, substitution with a tracheostomy tube instead of an endotracheal tube is known to lower the labor of breathing and clear the airway secretion better. The influence of different airway management approaches, like tracheostomy time on freedom from mechanical ventilation is indeterminate. Judging the perfect time for tracheostomy, either early or late,in acutely ill patients is known to be challenging and frequently subjective as per Andriolo et al. [26]

Pulmonary rehabilitation type and onset status on weaning

Pulmonary rehabilitation alongside early mobilization and physical therapy is considered asan efficient multidisciplinary approach to endorse effective weaning in patients under mechanical ventilation. Numerous authors stated advantages of pulmonary rehabilitation in mechanically ventilated patients embracing functionally enhanced status, period of free breathing trial, weaning frequency, and death rate.[27,28] Standard conventional rehabilitation programs are thus suggested in chronic acutely ill patients to hasten functionalrecovery and decrease ventilator dependence or weaning complications. However, reports on functional status correlation to standard pulmonary rehabilitation, weaning, and survival rate amongst patients who received mechanical ventilation are inadequate. Hypothetically, the functional status is as a factor of response to pulmonary rehabilitation. It must further be consistent and immediate predictor for weaning or survival, then mere acknowledgement of a rehabilitation program. All 62 participants received CPT since the beginning of mechanicalventilation. Out of the 62 participants, 42 patients additionally received PROM and the remaining 18 received AROM based on the clinical conditions. Among the study participants, 65% patients received an early onset pulmonary rehabilitation and 35% received a late onset pulmonary rehabilitation. However, no direct association was observed between the pulmonary rehabilitation program on weaning period. Our results were in agreement with another study which assessed the effect of early and late onset pulmonary rehabilitation in COPD patients in the study done by Puhan et al. [29]

Weaning and pulmonary rehabilitation

Weaning from mechanical ventilation is the procedure of gradually retreating ventilator support till the person could withstand unassisted breathing. Weaning is required to improve the respiratory muscles strength which in turn will resolve the underlying disease condition. Weaning at the earliest is a priority objective for relief from mechanical ventilation. Early weaning not only lessens ventilator-induced lung injury but also diminish the possibility of acquiring hospital sepsis, decrease patient uneasiness and necessity of sedatives, curtail the occurrence of oral aversion with succeeding feeding complications, and enable parental connection in the study done Taghva et al[30].

Weaning failure on the other hand is failure of spontaneous breathing trial or the necessity for reintubation within 48 hours subsequent to an extubation as per the study done by Esteban A et al [31] and Valverdú et al [32]. The majority patients who are unsuccessful with a series of weaning from mechanical ventilation report evidently elevated respiratory load, which is indicative of worsened respiratory mechanics during weaning trials. Infrequent explanationsfor weaning failure contain deteriorated respiratory muscles or diminished cardiovascular functioning, or prime anomalies in the intra-pulmonary shunt.

Current evidence report that about 70% of patients in the critical care could be weaned effectively within the first day. However, in 30% of the patients the initial efforts are unsuccessful with pertinent undesirable consequences in the weaning procedure in the study done by Heunks & van der Hoeven et al [33]. “Difficult-to-wean patients” necessitating lengthy mechanical ventilation, comprise for around 15% needful of mechanical ventilationin the critical care centers and around 25% of those acquire premature muscle weakness as per the study done by Boles et al. [34]

Conclusion

Although conclusive evidence could not be generated from the study about the association of early rehabilitation with weaning a gap in research till date has been identified. The researchshows that early weaning can be attained irrespective of tailored rehabilitation program, in contrary to certain studies which state that early intervention with a pulmonary rehabilitationaid in early weaning.

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