

Re-Intubation Among Critical Care Patients: A Scoping Review

Thandar Soe Sumaiyah Jamaludin¹, Mohd Said Nurumal^{1*}, Nur Syila Syahida Syaziman², Syuhada Suhaimi² & Muhammad Kamil Che Hasan¹

¹Kulliyah of Nursing, International Islamic University Malaysia, Pahang, Malaysia.

²National Heart Institute, Kuala Lumpur, Malaysia.

ABSTRACT

Objective: This paper aimed to identify relevant literature about what are the factors that contributing to the re-intubation and current intervention to overcome it among critical care patients. **Methods:** A scoping review was carried out with the 17 articles which publish with the year 2010 to 2021. The literature search was systematically done by using PRISMA flow diagram. The quality assessment was conducted by using Effective Public Health Practice Project (EPHPP) assessment tool and the authors applied inter-rater reliability for the included articles. Results: Four themes were emerged in this scoping review. Those were the criteria for extubation, factors of extubation failure and re-intubation, medical conditions associated with re-intubation, and intervention to reduce reintubation rate among critical care patients. **Conclusion:** The rate of re-intubation among critical care patients can be reduced when protective measures take place properly. Those are the use of non-invasive ventilation in between successful spontaneous breathing trials and extubation, the proper usage of analgesics and sedatives during extubation and monitoring the indicators like blood urea nitrogen and central venous pressure.

Keywords: Critical Care, Intubation, Extubation and Re-intubation

INTRODUCTION

Critical care settings especially intensive care unit (ICU) deals with patients who are having life-threatening diseases that require multiple intervention and continuous haemodynamic monitoring ⁽¹⁾. Hemodynamic monitoring is an important measure to ensure adequate tissue oxygen delivery and end organ perfusion by guiding the medical management to treat and improves the patient's conditions ⁽¹⁾. Moreover, patients who are in the critical care setting have problems with one or more organs and most of them are unable to breath their own ⁽²⁾. Thus, they required a mechanical ventilation or an invasive ventilation to support their breath.

According to the Malaysian Society of Intensive Care, the invasive ventilation admission was

recorded with 77.0% while non-invasive ventilation comprised 17.8% admissions in the critical care setting ⁽³⁾. They also reported that the re-intubation rate in critical care setting was 5.6% ⁽³⁾. Furthermore, extubation failure and re-intubation are associated with a high mortality rate of 25 – 50% and those patients have higher chance to re-admit to intensive care unit although they have been discharged to the ward (ICU) ⁽²⁻⁴⁾. A previous study found that the patients who require re-intubation usually have poor prognosis and the mortality rate is exceeding 30%–40% irrespective of the cause for re-intubation ⁽⁵⁾. Moreover, studies described that the re-intubated patients within 48 to 72 hours of their initial extubation have a higher mortality rate in critical care setting ^(3, 6 & 7). However, updated evidence-based interventions are required to revamp the medical management standard to improve patient outcomes and lowering the in-ICU mortality rates. Thus, this scoping review focused on the re-intubation and factors that are associated with it among critical care patients.

METHOD

This paper applied a scoping review method with the aimed to identify relevant literature about what are the factors that contributing to the re-intubation and current intervention to overcome it

* Corresponding author:

Assoc. Prof. Dr. Mohd Said Nurumal
Department of Critical Care Nursing,
Kulliyah of Nursing,
International Islamic University Malaysia,
Jalan Sultan Ahmad Shah, Bandar Indera Mahkota,
25200 Kuantan, Pahang, Malaysia.

Email: mohdsaid@iium.edu.my

Tel no: +6095707288

among critical care patients.

Literature search strategies

The articles included in this review were retrieved from the EBSCO, ProQuest, Scopus, NCBI and BMJ databases. Using Boolean phrase and the keywords used were "ICU OR critical care setting OR critical care unit", "reintubation AND extubation", "factor OR reason OR issue OR problem". The inclusion criteria for this review were the studies that conducted for extubation and reintubation procedure occur in critical care settings, the studied that published between the year 2015-2020, full-text articles, the studied that published in English language.

Literature search outcomes

The searching of literature was systematically done by using PRISMA flow diagram in this scoping review. A total of 1,973,965 articles from ProQuest, 200,446 articles from EBSCOhost Discovery, 8711 articles from Scopus, 533 articles from BMJ Journal and 5395 articles from NCBI were found at initial phase. Further screening process was done by the author and confirmed with the team members for quality assessment of the included articles. A total of 17 articles were chosen to be included in this scoping review and further analysis was carried out. Figure 1 shows the review of the literature process based on the PRISMA flow diagram.

Quality assessment

All the included 17 articles were screened by two authors independently. Disagreements were resolved between the two authors and if it was not solved other team members were also called for discussion in the review process. The authors used the key criteria for the quality assessment of the selected articles. Those were selection bias, study design, confounders, blinding, data collection methods, withdrawals and dropouts, intervention integrity, findings and recommendations for future study. The quality assessment was conducted by using Effective Public Health Practice Project (EPHPP) assessment tool and the authors applied inter-rater reliability for the included articles⁽⁸⁾. Based on previous study, if the authors obtained 0.6 of inter-rater reliability value which is considered as fair agreement among raters and if more than that considered excellent inter-rater reliability value⁽⁹⁾. In this scoping review, the authors obtained the inter-rater reliability value of 0.77 (95% CI) which was considered as excellent agreement between the reviewers.

FINDINGS

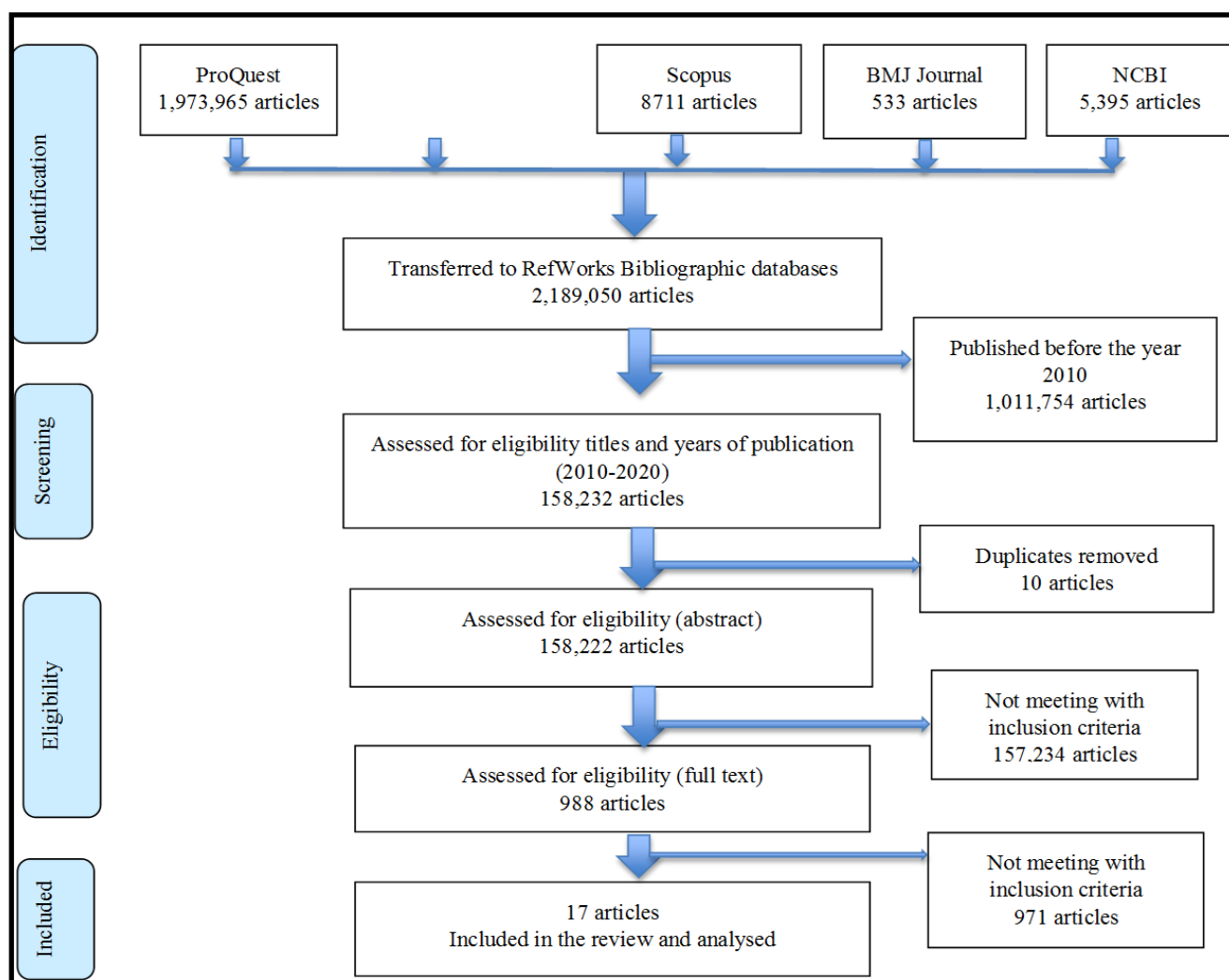
There were four types of study designs were found among the 17 articles. Those were two randomized control trial studies, six cohort studies, eight case-control studies, and one cross-sectional study. Their study settings also vary from one another. There were two studies from Thailand, two studies from Korea, one study that was conducted at China and Italy respectively, one study from Ecuador, one study from Spain, three studies from Singapore, one study from Pakistan, two studies from United States of America, one study from France and two studies from China. However, no previous study was found from Malaysia.

Four themes were emerged in this scoping review. Those were the criteria for extubation, factors of extubation failure and re-intubation, medical conditions associated with re-intubation, and intervention to reduce reintubation rate among critical care patients. The following sessions explained further about the emerged themes.

The criteria for extubation

The criteria for extubation will differ according to the hospital policy. Patients will be extubated if they passed the spontaneous breathing trial (SBT)⁽¹⁰⁾. Furthermore, weaning and physiotherapy protocols differ from each participating hospital hence the practices will be different since the study was conducted at 17 different Spanish medical-surgical intensive care units⁽¹⁰⁾. Another study also described that the patients will be directly extubated after SBT completion with the condition that respiratory rate ≤ 30 breaths/min, pH value ≥ 7.35 , carbon dioxide partial pressure (PaCO₂) ≤ 50 mmHg and Oxygen partial pressure (PaO₂) ≥ 70 mmHg with fraction of inspired oxygen (FiO₂) of 0.3, without dyspnea, respiratory accessory muscle recruitment and paradoxical abdominal motion⁽¹¹⁾. A study from Korea described that critical care patients who undergo SBT on low level of pressure support ventilation (ranging from +5 to +10 cmH₂O, Positive end expiratory pressure (PEEP) 4 – 5 cmH₂O) has a successful extubation rate compared to those patients who were not followed the said process⁽¹²⁾. Another study found that the patients were eligible for SBT will be ventilated with 5 cmH₂O of PEEP and pressure support before starting the SBT and the SBT was performed on "T-piece" that connected to the oxygen source for 1- or 2-hours duration will be decided by their attending physicians⁽¹³⁾. After that, those patients were extubated once they were successfully undergone the SBT period⁽¹³⁾.

PRISMA FLOW DIAGRAM



Besides, a post-operative weaning criteria includes hemodynamic stability whether no or decreasing use of cardio active drugs, absence of significant bleeding (<100 mL/h), absence of significant arrhythmias, adequate urine output (>1 mL/kg/h), oxygen saturation more than 95% with fractional concentration of inspired oxygen less than 0.50 and the patient also needed to be sufficiently awake to follow commands ⁽⁵⁾. The critical care patients will be extubated when they pass the SBT period and their hemodynamic is stable.

Factors of extubation failure and re-intubation

The extubation failure is highly correlated with re-intubation. Studies found that the re-intubation was commonly happened in critical care patients who have been extubated within 48 hours ^(6, 10-11 & 13-14). On the other hand, another study defined the re-intubation as the extubation failure as unplanned reintubation within 72 hours of extubation ⁽¹²⁾. The factors of re-intubation were 3 major reasons: cardiac, respiratory and thoracic ⁽⁵⁾. Highest rate of re-intubation is respiratory reason where patients get impending respiratory failure. Meanwhile for

cardiac patients, the reasons are because of cardiopulmonary arrest, pulmonary hypotension after combined valvular and CABG surgery and arrhythmia ⁽⁵⁾.

The factors of extubation failures also found in high risk patients: age >65 years, comorbidities >1, upper airway problems, COPD, APACHE II > 12, >1 failed SBT, copious secretions, BMI >30, and cardiac insufficiency, both in control and rest group ⁽¹⁰⁾. Another study found that extubation failures were common among overweight and obese patients with planned extubation, the frequent cause of extubation failures were a patient with hemodynamic instability, excess secretions, upper airway obstruction and encephalopathy ⁽⁷⁾. Extubation failures usually occur to patients with lower body temperature in which it reflects on the severity of the illness and have less physiologic reserve, patient with higher faces anxiety scale (FAS) and higher calcium level ⁽⁶⁾. Moreover, even though it was not statistically significant, the usage of steroid, inotropic agents and sedatives can be seen more in the patient with failed extubation ^(6 & 12). A retrospective study conducted among 15840

critical care patients in Taiwan found that reintubation rate is high in older patients, patients with comorbidities, district hospitals and public hospitals (15).

Another prospective observational study about predictive factors of reintubation in Thailand, identified that elevated blood urea nitrogen level, low hemoglobin level, and muscle weakness were identified as independent risk factors for reintubation (16). Unplanned extubation is also a significant risk factor for reintubation. Nearly 2.6% of study's patients experienced an unplanned extubation with a reintubation rate of 23.1% (12). Another factors for reintubation also because of longer duration of mechanical ventilation before extubation, initial intubation for respiratory reasons, initial intubation outside of the operating room setting and the use of NIV after extubation (17). Apart from that, reintubation risk is also associated with anaemia in which is defined either as serum haemoglobin levels <10 g/ dl or haematocrit <34% in prior studies (17). In addition, the environmental factors such as unplanned extubation usually occurred during night shift and with nurses with shorter career and experience (17).

Medical conditions associated with reintubation

As mentioned by previous study, there were 3 factors of reintubation which were cardiac, respiratory and thoracic (5). Weak patients have a higher risk of reintubation after spontaneous breathing trial (SBT) (10). Respiratory muscle exhaustion is an important criteria for diagnosing post-extubation respiratory failure because SBT can be demanding especially for critically ill patients (13). In addition, inability to manage secretions are also important risk factors for reintubation (10).

In a retrospective control study, it was stated that the factors that connected to the reintubation were when the patient had pneumonia and/or sepsis (12). In addition, the researchers also stated that if the initial reason for extubation was respiratory reason the patient will be likely to be reintubated (12). The common aetiologies of patients that experienced reintubation were pulmonary failures, cardiovascular failures and neurological failures (7). Moreover, diabetes mellitus and stroke were the common underlying comorbidities that associate with reintubation (7). Studies also found that failed extubation groups also have higher blood urea nitrogen (BUN) level and end stage renal failure (ESRD) (6&7). A study also found that patients who have pneumonia also lead to extubation failure (16).

Intervention to reduce re-intubation rate

Studies have suggested that 1 hour re-connection to the ventilator to rest after successful SBT period, the use of noninvasive ventilation (NIV) protocol extubation for periods of at least 1 hour, and with a minimal duration of 8 hours within the first 24 hours following extubation can reduce the re-intubation rate from 28% to 15% among critical care patients (10 & 18). Another study also suggested that proper usage of sedations and analgesics can reduce the asynchronization of patient and ventilator interface, thus reducing the oninvasive positive-pressure ventilation (NIPPV) failure, the re-intubation rate and mortality rate (19).

Moreover, NIV usage after extubation helped to reduce the usage of re-intubation risks (11). However, a study showed that NIV prophylactic after extubation only benefits to patients that have weak cough peak flow post extubation (13). Besides that, 1.0 g/dl difference in median hemoglobin levels of critical care patients were not associated with extubation failure, however it is wise to note that the role of anemia as the markers for disease severity and respiratory failure (12). A study also suggested that there were top three predictors for successful extubation in critical care patients which were rapid shallow breathing index (RSBI), respiratory rate and minute ventilation (14).

DISCUSSION

Based on this scoping review findings, there are few aspects that can be taken into consideration as key indicators to prevent the rising trends in rate of re-intubation among critical care patients. The following sessions will describe further about discussion.

Criteria for extubation

Studies have described that the higher blood urea nitrogen (BUN) level was associated with extubation failure among critical care patients (6 & 7). The BUN measures the amount of urea in the blood and indicates kidney function of the patients (20). The higher BUN level was associated with risk of kidney disease progression and was useful for renal outcomes prediction in ventilated patients (21). This suggested that good kidney prognosis can predict the success of the extubation among critical care patients.

Another study suggested that the abnormal rise in central venous pressure during spontaneous breathing trial (SBT) was associated with extubation failure (13). Cardiac patients were at risk for extubation failure due to abrupt burden for the

cardiovascular system (14). This was supported by a study saying that one of the common etiologies of reintubation was cardiovascular failures (7, 22). Moreover, the higher BUN level was associated with cardiovascular mortality in patients with acute heart failure (23). Therefore, it is suggested to consider the findings above as the indicators of criteria for extubation to decrease the risk of re-intubation, improve the rate of mortality and the length of hospital stays among critical care patients.

Factors of extubation failure and reintubation

Studies have shown that advanced age seems to be highly correlated with extubation failure (21-22). The reason might be due to poor underlying health condition or comorbidity that they have prior to the hospital admission such as COPD, hypertension and hyperglycemia. Moreover, extubation failures usually occur to patients with lower body temperature in which it reflects on the severity of the illness and have less physiologic reserve, patient with higher faces anxiety scale (FAS) and higher calcium level (6). A study also found out that the difference level of haemoglobin is not associated with extubation failure (12). This finding was opposite from a study which they found that higher haemoglobin levels were associated with weaning success (24). In addition, haemoglobin involves in oxygen delivery that affect the cardiac workload, breathing and respiratory muscle endurance (24 & 25). Besides, patients with SBT failure have increase in haemoglobin values which indicate that SBT induced higher haemoglobin and haematocrit values (14 & 25). However, patients with red blood cell transfusion were associated with severity if diseases thus can give insight about further prognosis (25). Thus, we need to monitor the haemoglobin level in critical care patients before the extubation take place.

Medical conditions associated with reintubation

Medical conditions such as pneumonia, and cardiac failure were common cause for re-intubation among critical care patients (5 & 14). This was supported by a recent study stated that severe pneumonia patients were likely to have extubation failure (21). This can be indicated by APACHE II score > 17.5, blood glucose > 9.87 mmol/l, fentanyl usage > 1.135 mg/d, and the need for RBC transfusion might be associated with higher risk of extubation failure (21).

Study also shown that the patient with lower body temperature associated with disease severity (6). Patient with low temperature or hypothermia can lead to coagulopathy which can be hard to be detected since lab assays run in body normal temperature (23 & 24). Furthermore, it also associated with longer hospital stays, requirement for blood

transfusion and increase risk of cardiac diseases which will ultimately affect the quality of life of patients (24 & 26-27). Additionally, patients with fever were associated with less likelihood to successful weaning from ventilator (26 & 28). The study also found out that patient with hypothermia also associated with decreased ventilator-free days and higher mortality rate (26). Thus, assessing the underlying medical conditions of critical care patients is important.

Intervention to reduce re-intubation rate

The re-intubation can be prevented if there is intervention done before or after the extubation. The intervention might be the use of non-invasive ventilation such as venturi mask or the use of correct sedatives and analgesics during the extubations. A previous randomized control study was conducted among critical care patients (10). They have formed control group and rest group. The control group was extubated straight after a successful spontaneous breathing trial (SBT). Meanwhile the rest group was given a 1 hour reconnection to a mechanical ventilator before extubation. Their results showed that reintubation within 48 hour post extubation was common in the control group rather than the rest group (10). This could be due to the SBT period. SBT can be hard work for critically ill patients which could lead to diaphragm muscle fatigue. Thus, the reconnection to mechanical ventilators after a tired SBT helps the muscle to relax and prepare for extubation.

Studies also shown that usage of NIV after extubation reduce the risk of re-intubation among critical care patients (23 & 28). Another intervention used to reduce risk of re-intubation is the use of analgesics and sedatives during extubation especially if the patient undergoes unplanned extubation (17 & 29). Moreover, patients with unplanned extubation have significantly higher incidents of pain and lower sedation levels which likely to cause delirium (17). In order to manage the interface intolerance of extubation, administering the sedatives (dexmedetomidine, propofol) or analgesia (fentanyl, sufentanyl) to patients that develop NIPPV asynchrony in which ultimately decrease the failure of NIPPV trial (24 & 29).

According to their hypothesis, analgesics and sedatives can reduce the rate of delirium, relieve anxiety, and stimulate patients to sleep. Physiologically, the body stress response such as hypertension and tachycardia can be modulated in which improve the respiratory status. It also reduced patient's use of NIPPV. Therefore, we need to focus monitoring about cardiovascular function by monitoring the central venous

pressure and neurological status of patients after starting SBT so that appropriate intervention can be taken.

LIMITATION

There is limited study conducted on intervention to improve the rate of successful extubation. In addition, there is very limited study on this particular topic especially in Malaysia. Even though there is evidence and study in the Southeast Asia region, the demographic will be different and will eventually affect the study results. The study for the indicator that predicted extubation failure is widely available however there is no specific research on the effectiveness of it.

CONCLUSION

The rate of extubation failure and re-intubation is still considerably high among critical care patients. It was associated with failed spontaneous breathing trials, severity of medical conditions of patients and environmental factors such as experience of staff. Re-intubation can lead to longer hospital stay and higher mortality rate. However, it can be reduced with several prophylactic interventions such as the use of non-invasive ventilation in between successful spontaneous breathing trials and extubation, the use of analgesics and sedatives during extubation and monitoring the indicators like blood urea nitrogen and central venous pressure. Future studies that focus on intervention to reduce re-intubation incidents should be conducted. Studies for extubation and re-intubation should also include the assessment of nurses and physicians in handling extubated patients as external factors.

CONFLICT OF INTEREST

Authors declare there is no conflict of interest in this study.

REFERENCES

1. Malbrain MLNG, Huygh J, Peeters Y & Bernardis J. Hemodynamic monitoring in the critically ill: An overview of current cardiac output monitoring methods. *F1000Research*. 2016; (5): 1–9. <https://doi.org/10.12688/f1000research.8991.1>
2. NHS. Intensive Care. 2019; <https://www.nhs.uk/conditions/intensive-care/>.
3. Malaysia Society of Intensive Care. Welcome to MSIC. 2017; Retrieved March 2020, from <http://www.msic.org.my/>.
4. Jamaludin TSS, Suhaimi NS, Mohd Noor H & Nurumal MS. Intensive Care Unit (ICU) Readmission: A Mixed- Method Systematic Review. *International Journal of Care Scholars* 2021; 4(2).
5. Siddiqui KM, Samad K, Jonejo F, Khan MF & Ahsan K. Factors affecting reintubations after cardiac and thoracic surgeries in cardiac intensive care unit of a tertiary care hospital. *Saudi journal of anaesthesia*. 2018; 12(2), 256.
6. Suraseranivong R, Krairit O, Theerawit P & Sutherasan Y. Association between age-related factors and extubation failure in elderly patients. *PLoS ONE*. 2018; 13(11), 1–11. <https://doi.org/10.1371/journal.pone.0207628>.
7. Chao CM, Lai CC, Cheng AC, Chiang SR, Liu WL, Ho CH, Cheng KC. Establishing failure predictors for the planned extubation of overweight and obese patients. *PLoS ONE*. 2017; 12(8), 1–11. <https://doi.org/10.1371/journal.pone.0183360>
8. Effective Public Health Practice Project (EPHPP). Quality Assessment Tool for Quantitative Studies. 2021; Retrieved on 6th November 2021. <https://www.ehpp.ca/quality-assessment-tool-for-quantitative-studies/>
9. Armijo-Olivo S, Stiles CR, Hagen NA, Biondo PD, Cummings GG. Assessment of study quality for systematic reviews: a comparison of the Cochrane Collaboration Risk of Bias Tool and the Effective Public Health Practice Project Quality Assessment Tool: methodological research. *Journal of evaluation in clinical practice*. 2012;18(1):12–8.
10. Fernandez R. Reconnection to mechanical ventilation for 1 h after a successful spontaneous breathing trial reduces reintubation in critically ill patients: a multicenter randomized controlled trial. *Intensive Care Medicine*. 2017; 43(11), 1660–1667. <https://doi.org/10.1007/s00134-017-4911-0K>.
11. Vaschetto R, Longhini F, Persona P, Ori C, Stefani G, Liu S, Navalesi P. Early extubation followed by immediate noninvasive ventilation vs. standard extubation in

- hypoxemic patients: a randomized clinical trial. *Intensive Care Medicine*. 2019; 45(1), 62–71. <https://doi.org/10.1007/s00134-018-5478-0>.
12. Lee AL, Chung CR, Yang JH, Jeon K, Park CM & Suh GY. Factors Affecting Invasive Management after Unplanned Extubation in an Intensive Care Unit. *The Korean Journal of Critical Care Medicine*. 2015; 30(3), 164–170. <https://doi.org/10.4266/kjccm.2015.30.3.164>.
 13. Dubo S, Valenzuela ED, Aquevedo A, Jibaja M, Berrutti D, Labra C, Castro R. Early rise in central venous pressure during a spontaneous breathing trial: A promising test to identify patients at high risk of weaning failure? *PLoS ONE*. 2019; 14(12), 1–11. <https://doi.org/10.1371/journal.pone.0225181>.
 14. Tu CS, Chang CH, Chang SC, Lee CS & Chang CT. A Decision for Predicting Successful Extubation of Patients in Intensive Care Unit. *BioMed Research International*. 2018; <https://doi.org/10.1155/2018/6820975>.
 15. Chu CC, Liu CJ, Yen SM, Chou WY, Kung PT, Tsai YS & Tsai WC. Factors associated with re-intubation within 14 days after ventilator liberation. *Respiratory Care*. 2017; 62(12), 1557-1564.
 16. Piriypatsom A, Williams EC, Waak K, Ladha KS, Eikermann M & Schmidt UH. Prospective observational study of predictors of re-intubation following extubation in the surgical ICU. *Respiratory Care*. 2016; 61(3), 306-315
 17. Kwon EO & Choi KS. Case-control Study on Risk Factors of Unplanned Extubation Based on Patient Safety Model in Critically Ill Patients with Mechanical Ventilation. *Asian Nursing Research*. 2017; 11(1), 74–78. <https://doi.org/10.1016/j.anr.2017.03.004>.
 18. Thille AW, Boissier F, Ben-Ghezala H, Razazi K, Mekontso-Dessap A, Brun-Buisson C & Brochard L. Easily identified at-risk patients for extubation failure may benefit from noninvasive ventilation: a prospective before-after study. *Critical Care*. 2016; 20(1),
 19. El Hadidy S, Saad M, El Hossany R, El Gohary T & El Ghobashy M. Coinciding Changes in B Lines Patterns, Haemoglobin and Hematocrit Values Can Predict Outcomes of Weaning from Mechanical Ventilation. *Open access Macedonian journal of medical sciences*. 2019; 7(23), 4010–4014. <https://doi.org/10.3889/oamjms.2019.615>.
 20. Hsiung Lee ES, Jiann Lim DT, Taculod JM, Sahagun JT, Otero JP, Teo K, et al. Factors associated with reintubation in an intensive care unit: A prospective observational study. *Indian J Crit Care Med* 2017;21:131-7.
 21. Yu H, Luo JN, Hu Y, Liu D, Wang M & Liang Z. Early prediction of extubation failure in patients with severe pneumonia: a retrospective cohort study. *Bioscience Reports*. 2020; 40(2).
 22. Buppha P, Kusumaphanyo C & Chittawatanarat K. Outcomes and risk factors of extubation failure: a multicenter study of the THAI Surgical Intensive Care Units (SICUs). *J Med Assoc Thai*. 2016; 99 (suppl 6), S136-S144.
 23. Thomrongpairroj P, Tongyoo S, Tragulmongkol W & Permpikul C. Factors predicting failure of noninvasive ventilation assist for preventing reintubation among medical critically ill patients. *Journal of Critical Care*. 2017; 38, 177-181.
 24. Lai YC, Ruan SY, Huang CT, Kuo PH & Yu CJ. Hemoglobin levels and weaning outcome of mechanical ventilation in difficult-to-wean patients: a retrospective cohort study. *PLoS one*. 2013; 8(8), e73743. <https://doi.org/10.1371/journal.pone.0073743>.
 25. Ghiani A, Sainis A, Sainis G. et al. Anemia and red blood cell transfusion practice in prolonged mechanically ventilated patients admitted to a specialized weaning center: an observational study. *BMC Pulm Med*. 2019; (19), 250. <https://doi.org/10.1186/s12890-019-1009-1>.
 26. Netzer G, Dowdy DW, Harrington T, Chandolu S, Dinglas VD, Shah NG, Colantuoni E, Mendez-Tellez PA, Shanholtz C, Hasday JD & Needham DM. Fever is associated with delayed ventilator liberation in acute lung injury. *Annals of the American Thoracic Society*. 2013; 10(6), 608–615. <https://doi.org/10.1513/AnnalsATS.201303-052OC>.
 27. Jamaludin TSS & Chong CM. Influence of Perceive Social Support or Pre-Operative Support Program on Quality of Life in Patients Awaiting Coronary Artery Bypass Grafting (CABG) Surgery: Mixed Method

Systematic Review. International Journal of Care Scholars 2019;2(1).

28. Duan J, Han X, Huang S & Bai L. Noninvasive ventilation for avoidance of reintubation in patients with various cough strength. *Critical Care*. 2016; 20(1), 316.
29. Elmer J, Lee S, Rittenberger JC, Dargin J, Winger D & Emlet L. Reintubation in critically ill patients: procedural complications and implications for care. *Critical Care*. 2015; 19(1), 12.