Comparison of Early Mobilization Protocols on Postoperative Cognitive Dysfunction, Pain, and Length of Hospital Stay in Patients Undergoing Coronary Artery Bypass Graft Surgery: A Randomized Controlled Trial

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Abstract

Although coronary artery bypass graft (CABG) surgery improves the life expectancy of patients with coronary artery disease, it is associated with various short and long-term complications. Early mobilization has been shown to reduce the risk of these complications. This study aimed to compare the effectiveness of different early mobilization protocols on postoperative cognitive dysfunction (POCD), pain intensity, and length of hospital stay (LOS) in patients undergoing CABG. This three-arm parallel randomized controlled trial included 120 patients undergoing CABG surgery who were randomly assigned to Intervention A, which received a four-phase early mobilization protocol; Intervention B, which received a three-phase early mobilization protocol; and the Control group, which received routine care. Postoperative cognitive dysfunction and pain were assessed using Mini Mental State Examination (MMSE) and visual analog scale (VAS), respectively. Groups were comparable in demographic and clinical characteristics and postoperative cognitive dysfunction at baseline. After the intervention, Group B had statistically significantly ($p<0.001$) less cognitive dysfunction (25.8±1.7) compared to Group A (24.1±2.2) and the Control Group (23.4±2.7). Likewise, hospital stay was statistically ($p<0.01$) shorter for Group B (7.7±1.5) than the Control group (8.9±1.9). However, the experience of pain was statistically significantly lower over time in Group A than in the other groups ($p<0.001$). This study concludes that an early mobilization protocol based on deep breathing exercises and chest physiotherapy may better improve postoperative cognitive dysfunction and length of hospital stay than an early mobilization protocol based on passive and active range of motion activities or routine care.

Keywords: CABG, early mobilization, length of hospital stay, pain, postoperative cognitive dysfunction, intensive care unit

Introduction

Despite the beneficial effects of Coronary Artery Bypass Graft surgery (CABG) on patients' symptoms, survival rate, and quality of life, complications are common in the short and long term after the procedure (Subramanian et al., 2019). During the initial postoperative phase in the intensive care unit (ICU), patients may experience a range of complications, including arrhythmias, bleeding, myocardial infarction, wound infections, pain, and pulmonary complications (Pooria et al., 2020). These post-surgery complications increase the risk of morbidity, mortality (Hardiman et al., 2022), and lengthen the stay in the ICU and hospital (Zarrizi et al., 2020). The prolonged stay in the ICU is also a predictor of higher morbidity and long-term mortality after cardiac surgeries (Mahesh et al., 2012).

According to estimates, between 50-70% of patients in the ICU experience cognitive impairment, and 60-80% develop ICU-acquired weakness, which can delay functional recovery and prolong hospitalization (da Costa Torres et al., 2016; Wischmeyer & San-Millan, 2015). Cognitive impairment is a common complication following surgery, and patients who have undergone CABG are at a higher risk for this condition (Greaves et al., 2019). A systematic review and meta-analysis found that approximately 43% of patients experience cognitive impairment after CABG, and around 40% suffer from this complication in the long term, from 1 to 5 years after the surgery (Greaves et al., 2019). Postoperative cognitive impairment refers to a reduction in a patient's ability to orient themselves, pay attention, perceive things, maintain consciousness, and make judgments (Kotekar et al., 2018). Patients who are older, female, experience higher levels of bleeding, or have elevated creatinine levels after surgery are at a greater risk of developing postoperative cognitive impairment (Habib et al., 2014).

The specific cause of postoperative cognitive decline is not fully understood, but it is believed to be related to the body's stress and inflammatory response to surgery and anesthesia (Cusack & Buggy, 2020). The excessive release of inflammatory factors, such as Glial fibrillary acidic protein (GFAP) may cause neuronal dysfunction, which can result in postoperative cognitive decline (Traub et al., 2022). Furthermore, respiratory muscle weakness, reduced cardiac output (Cassina et al., 2016), and anaerobic metabolism are common complications of CABG that can lead to cerebral hypoxia, contributing to postoperative cognitive impairment (Klypa et al., 2016; Nydahl et al., 2020). Pain and analgesic medication use can also lead to cognitive impairment in these patients (Ochroch et al., 2021). Postoperative cognitive dysfunction can persist for an extended period, negatively impacting a patient's daily functioning and quality of life, and even leading to mental health disorders and death (Nydahl et al., 2020).

Early mobilization is crucial for improving patient outcomes following CABG (Marra et al., 2017; Nydahl et al., 2020), and it is now widely implemented in hospitals (Harris & Shahid, 2014). This intervention has been shown to be safe and effective in improving tissue perfusion, maintaining muscle tissue strength and mass (Roberson et al., 2018), reducing pulmonary complications and hospital stay length (Brown et al., 2018), enhancing quality of life (Alqahtani et al., 2022), and lowering mortality rates (Kanejima et al., 2020). Furthermore, early mobilization has been demonstrated to be effective in reducing delirium (Kress & Hall, 2014), which is a significant risk factor for ICU-related cognitive impairment (Marra et al., 2017). Various early mobilization interventions are available for patients following surgery, and while most are effective in improving outcomes, the most effective protocols have not yet been identified. This study aims to compare the effectiveness of two different early mobilization interventions in improving CABG patients' cognitive impairment, pain experience, and length of hospital stay.

Methods

This randomized controlled trial was conducted with three parallel groups consisting of two interventions and one control group. Participants in intervention group A received a four-phase intervention, while those in intervention group B received a three-phase intervention. Participants in the control group received only routine care.

Study setting and participant recruitment

During the period of 12 October to 10 November 2019, this study was conducted in the intensive care unit of Shahid Madani Cardiovascular Centre, which is affiliated with Tabriz University of Medical Sciences in Iran. Participants were selected from the cardiac surgery wards of the cardiovascular center while they were waiting for their CABG surgery. To be included in the study, the participants had to be between 18 and 65 years of age, a candidate for CABG, have a BMI of 20-30 kg/m2, mean arterial blood pressure between 60-100, heart rate between 60-100, respiratory rate between 12-20, and agree to participate in the research. Patients were excluded from the study if they underwent an urgent CABG, had a history of previous open-heart surgery or psychological or neuromuscular problems (such as cognitive dysfunction or paralysis) as per their medical records, were hemodynamically unstable or on inotropic drugs, had arrhythmia, unstable angina, or respiratory distress. Additionally, patients with a decreased level of consciousness, mitral valve repair or replacement during the index CABG surgery, cardio-respiratory arrest during the surgery or after admission to ICU, oxygen saturation below 90%, left ventricular ejection fraction below 40%, mechanical ventilation for more than 24 hours post-surgery, chest tube drainage more than 100 ml within the first four hours after surgery, and those who received analgesics or neuromuscular-blocking agents after admission to ICU were excluded from the study.

Sample size calculation and randomization

The study's sample size was calculated using G*power 3.1.2 software. A pilot study involving 30 participants was conducted to aid in calculating the required sample size. Based on the between-group difference in cognitive dysfunction on the second evening, α=0.05, and a power of 95%, 32 participants were required for each study arm. To account for an attrition rate of 25%, 40 participants were recruited for each study arm (Figure 1).

Patients who met the study's inclusion and exclusion criteria were screened at the cardiac surgery wards of the participating cardiovascular center. Eligible patients received information about the study and its objectives, and those who consented to participate were randomly assigned to one of the three study arms at a ratio of 1:1:1. Random numbers were generated using a random number generator by an independent person who also prepared the sequentially numbered sealed opaque allocation envelopes. The researcher providing the study interventions was informed of each participant's allocation after their CABG surgery when they were admitted to the ICU. The outcome assessor and data analyst were blinded to the group allocations. Participants were placed in their respective ICU units without any interaction between them.

Interventions

Participants in Group A received a four-phase early mobilization intervention

, which emphasized range of motion exercises and was adapted from previous studies (Morris et al., 2008; Ziyaeifard et al., 2018). In Phase I, participants received passive range of motion exercises twice daily, ten times in each cycle, with the head of the bed elevated to 30 degrees for 15 minutes, and their position was changed in the bed every two hours. If tolerated by the participant, they proceeded to Phase II, where they were instructed to perform active range of motion exercises twice daily, ten times in each cycle, with the head of the bed elevated to 45 degrees for 15 minutes and then to 90 degrees for the next 15 minutes, if tolerated. In Phase III, the researcher helped the participant sit at the edge of the bed with their feet hanging for 15 minutes. In Phase IV, the participant was transferred to a bedside chair by a nurse, rested for a few minutes, and was then assisted to walk in the ward up to 20 meters, depending on their tolerance.

Participants in Group B received a three-phase early mobilization intervention that focused on chest physiotherapy and deep breathing exercises, adapted from the study by Tariq et al. (2017). In Phase I, the head of the bed was elevated to 30 degrees for 3 minutes, and the participant was encouraged to perform deep breathing exercises, including breathing in through the nose, holding the breath for 3 seconds, and breathing out slowly through pursed lips while pressing gently on their abdomen. The participant then performed bottle-blowing exercises for the next 2 minutes, followed by chest physiotherapy consisting of chest percussion using clapping on the chest, back, and area under the arms for 5 minutes. The participant was then encouraged to cough to remove airway secretions while protecting their suture line with a pillow. If Phase I was well-tolerated by the participant, the researcher moved to Phase II, which involved raising the head of the bed to 45 degrees for 3 minutes and assisting the participant in sitting on the edge of the bed with their feet dangling for five minutes. If Phase II was tolerated, the participant moved to Phase III, where they sat on a bedside chair for a few minutes before standing up and completing ten steps of static walking.

Participants in the Control group received routine care, which included encouragement to mobilize as soon as they were able. The mobilization process began with assisting participants in sitting over the side of the bed with their feet hanging off for a few minutes. They were then assisted to sit on a bedside chair and, when ready, walked in the ward with assistance, depending on their tolerance. Control group participants did not receive the range of motion exercises or chest physiotherapy provided in Groups A and B.

The interventions for all groups started on day zero (the day of surgery), after participants had regained full consciousness (had a Glasgow Coma score of ≥14, were aware of time, place, and person), and were extubated, approximately 6-8 hours after surgery. The interventions continued on the following day (day one). Each participant received a total of four sessions of early mobilization intervention, twice daily on day zero and day one post-surgery. The interventions were provided around 10 am and 5 pm to avoid interfering with ward rounds, visiting hours, and shift changes.

During the interventions, the researcher continuously monitored the participant's heart rate and oxygen saturation using a portable pulse oximetry device. They also ensured the integrity of drainage lines and catheters and confirmed the participant's tolerance by questioning them. The study outcomes included the improvement in cognitive impairment, pain intensity, and length of hospital stay.

Data Collection

Demographic and clinical information was collected from medical records and participant interviews (Table 1).

The Mini Mental State Examination (MMSE)

The Persian version of MMSE was used to assess cognitive impairment. The MMSE is a widely used tool in clinical settings and research to assess cognitive impairment, including problems with thinking, communication, understanding, and memory. It consists of 11 questions and takes approximately 10 minutes to administer. The maximum score is 30, and higher scores indicate better cognitive functioning. The MMSE is commonly used as a screening tool to detect cognitive impairment, assess the severity of the impairment, or monitor changes in cognitive status over time (Tatari et al., 2011).

The Visual Analogue Scale (VAS)

Pain level was assessed using the Visual Analogue Scale (VAS), which is a validated and subjective tool for assessing acute and chronic pain (Myles et al., 2017). In this study, we used a 10-cm VAS consisting of a straight line with the endpoints indicating 0 (no pain) and 10 (unbearable pain). Scores 1-3 indicated mild pain, 4-7 moderate pain, and 8-10 severe pain

(Myles et al., 2017). To help participants mark their pain more accurately, we also included faces ranging from smiling to frowning faces, especially as they were likely to experience some level of cognitive impairment after CABG.

Before using the data collection tools in the study, we sought face and content validity by having ten faculty members review them.

Ethical considerations

The study received research ethics approval, IR.TBZMED.REC.1398.613 was registered in the Iranian Clinical Trial Registration Centre (IRCT20160110025937N5). The researchers explained the study and its objectives to participants while waiting for surgery in the cardiac surgery wards. Written informed consent was obtained for all participants. They were aware of the voluntary nature of the research and could withdraw from the study without concern.

Data analysis

Data analysis was performed using statistical software (e.g., IBM SPSS Statistics, R, etc.). Normality of variables was assessed using the Kolmogorov-Smirnov test. Differences between groups were analyzed using one-way ANOVA and chi-square/Fisher exact tests for continuous and categorical variables, respectively. Post hoc analyses were conducted using the Tukey-HSD test with a significance level set at 0.05. Any additional statistical methods used in the analysis should be mentioned here.

Results

The participant flow is illustrated in Figure 1. All participants who were randomized to the study groups completed the study. Their demographic and clinical characteristics are shown in Table 1. The groups were comparable at baseline.

Postoperative cognitive dysfunction

As presented in Table 2, the three groups were similar in terms of postoperative cognitive dysfunction experience at baseline. However, after interventions, a significant difference was observed between the groups ($p<0.001$); participants in Intervention Group B (25.8±1.7) had significantly lower postoperative cognitive dysfunction compared to Group A (24.1±2.2) and Control Group (23.4±2.7). Examining the sub-scores of the MMSE, no significant differences were found across groups in orientation, documentation, attention and calculation, formation, and short memory. However, the groups were significantly different in their language skills and ability to understand; participants in Intervention Group B (3.2±0.5) had a better ability to understand compared to those in Intervention Group A (2.5±0.6) and Control Group (2.6±0.7). Additionally, participants in Intervention Group B (3.2±0.5) showed higher language skills than Intervention Group A (2.6±0.7) and Control Group participants (2.5±0.6).

Pain

The study measured the participants' experience of pain at 12 different time points, as presented in Table 3. The baseline measurements showed that the experience of pain was similar across all groups ($p=0.88$). As time progressed, all groups experienced an improvement in their pain levels, with no significant differences between the groups at any specific time point.

However, the study found significant time and group interaction effects, indicating that the experience of pain was consistently lower in group A compared to the other groups over time and with repeated intervention ($p<0.001$).

Length of Hospital Stay (LOS)

The results of the study indicate that there was a significant difference in the length of hospital stay ($p=0.01$) among the groups (Table 4). Specifically, participants in Group B (7.7± 1.5) stayed significantly fewer days in the hospital compared to the Control group participants (8.9±

1.9). However, there was no statistically significant difference in the length of hospital stay between the two intervention groups (p=0.18).

Discussion

This study is the first to compare the effects of early mobilization based on passive and active range of motion activities with early mobilization based on deep breathing exercises and chest physiotherapy. The results indicate that both early mobilization interventions effectively improved the cognitive dysfunction of participants post-CABG surgery, which is consistent with previous research. Early mobilization has been reported to consistently improve ICU patients' cognitive functioning (MacKenzie et al., 2016) and after CABG surgery (Shirvani et al., 2020; Ziyaeifard et al., 2018). Additionally, early mobilization improves functional capacity, preventing neuromuscular and cognitive impairments (Le et al., 2021). It is possible that the beneficial effect of early mobilization on cognitive impairment is due to improved cerebral hypoxia. Early mobilization can also improve the efficiency of the respiratory system, including respiratory mechanics, pulmonary immune factors, airway clearance, and airflow resistance (Alaparthi et al., 2020). Moreover, early mobilization has been shown to be effective in reducing ICU patients' delirium (Kress & Hall, 2014), which is a leading risk factor for ICU-related cognitive impairment (Marra et al., 2017).

The results of the current study indicate that the early mobilization intervention based on deep breathing exercises and chest physiotherapy was more effective in reducing postoperative cognitive impairment in patients after CABG than early mobilization based on passive and active range of motion activities. This finding may support the hypothesis that the beneficial effect of early mobilization on cognitive improvement is due to the improvement of cerebral hypoxia, as mobilization based on deep breathing and chest physiotherapy has been found to be more effective in improving pulmonary parameters than mobilization based on range of motion activities (Esmealy et al., 2023). Additionally, Ferreira et al. (2015) reported that breathing exercises could improve cognitive functioning in the elderly, further supporting the use of respiratory exercises as a non-pharmacological intervention to improve cognitive function after CABG surgery.

The experience of pain improved in all groups over time and with repeated interventions, which is consistent with previous studies reporting improved pain levels on day one compared to day zero post-CABG (Totonchi et al., 2014). However, the improvement in pain was more pronounced in the early mobilization based on passive and active range of motion activities group compared to the routine care and early mobilization based on deep breathing exercises and chest physiotherapy group. Several studies have reported the beneficial effect of early mobilization on post-surgery pain (Cacau et al., 2013; Dehghani et al., 2020; Irman & Darma, 2020), possibly because early mobilization increases tissue perfusion and provides ample nutrition at the surgical site, promoting wound healing and pain relief (Nydahl et al., 2020; Seventina, 2020). Additionally, an increase in serotonin production following mobilization activities may reduce the experience of pain, or patients may be distracted from focusing on pain and their attention is drawn to mobilization activities (Seventina, 2020).

The reason why patients who received early mobilization based on passive and active range of motion activities reported more improvement in pain compared to patients who received early mobilization based on deep breathing exercises and chest physiotherapy may be due to the chest physiotherapy causing some pain in participants. It is suggested that percussion should be performed vigorously, yet should not be painful (Balachandran et al., 2005).

Early mobilization based on deep breathing and chest physiotherapy was found to be effective in reducing the length of hospital stay in patients after CABG surgery. This finding is consistent with most previous research, including studies by Hunter et al. (2020) and Ronnebaum et al.

(2012). The reduction in hospital stay may be partially attributed to a greater improvement in cognitive impairment observed in this group, as patients with cognitive impairment tend to have extended hospital stays. Additionally, early mobilization based on deep breathing exercises and chest physiotherapy may have reduced pulmonary complications, which could lead to a decreased length of hospital stay. This outcome is particularly important as a longer hospital stay is associated with increased healthcare complications, such as hospital-acquired infections, myopathy, neuropathy, immobility, worsening of cognitive status, as well as increased healthcare costs and mortality (Hunter et al., 2020; Ronnebaum et al., 2012).

Study strengthens and limitations

The strength of this research lies in the utilization of a randomized controlled trial design and the use of blinded data analysts. However, it is important to note that this study was conducted at a single center, and the researchers and patients were not blinded to group allocations, which may have introduced some bias into the study. Due to the nature of the intervention (four-phase early mobilization intervention vs. three-phase early mobilization intervention), it was not feasible to blind the researcher who provided the intervention. Additionally, employing a blind data collector was not possible as the data needed to be collected immediately before, immediately after, and 15 minutes after the intervention.

Furthermore, due to ethical considerations, routine early mobilization activities could not be eliminated from the control group. We employed the MMSE to evaluate cognitive status and monitor changes throughout the intervention course. The MMSE was selected for its extensive use among healthcare professionals to quickly assess cognitive status and identify potential impairments. Moreover, the tool had been validated and widely utilized within the Iranian population. For future studies of a similar nature, researchers may consider incorporating more comprehensive assessment tools like the Wechsler Adult Intelligence Scale (WAIS) or

Addenbrooke's Cognitive Examination (ACE) for longer follow-ups, enabling a more in-depth understanding of the cognitive abilities of their research participants.

Conclusions

In conclusion, this study provides valuable insights into the effects of early mobilization interventions on patients after CABG surgery. The findings indicate that early mobilization, regardless of the specific approach, effectively improves cognitive dysfunction in post-CABG patients, consistent with previous research. Moreover, early mobilization based on deep breathing exercises and chest physiotherapy appears to be more effective in reducing postoperative cognitive impairment compared to mobilization based on passive and active range of motion activities. This suggests that the beneficial impact of early mobilization on cognitive improvement may be linked to improved cerebral hypoxia.

Furthermore, the study reveals that patients receiving early mobilization based on passive and active range of motion activities reported greater improvement in pain compared to those undergoing deep breathing exercises and chest physiotherapy. It is worth noting that chest physiotherapy may induce some discomfort or pain in participants, potentially influencing pain perceptions. Another significant finding is that early mobilization based on deep breathing and chest physiotherapy leads to a reduction in the length of hospital stay for post-CABG patients, aligning with previous research. This reduction may be attributed to the greater improvement in cognitive impairment observed in this group and the potential mitigation of pulmonary complications.

These findings underscore the importance of incorporating early mobilization interventions into post-CABG care protocols. Deep breathing exercises and chest physiotherapy, in particular, emerge as promising non-pharmacological interventions for improving cognitive function and shortening hospital stays in this patient population. However, it is crucial to consider the individual patient's needs and preferences when selecting the appropriate early mobilization strategy.

Overall, the results of this study contribute to the growing body of evidence supporting the positive impact of early mobilization on postoperative outcomes after CABG surgery. Healthcare providers should continue to prioritize and implement early mobilization practices to enhance patient recovery, reduce postoperative complications, and improve overall outcomes for individuals undergoing CABG surgery. Further research and larger-scale studies are warranted to better understand the underlying mechanisms and refine early mobilization strategies to optimize patient care and rehabilitation.

References

Alaparthi, G. K., Gatty, A., Samuel, S. R., & Amaravadi, S. K. (2020). Effectiveness, safety, and barriers to early mobilization in the intensive care unit. *Critical care research and practice*, *2020* .

Alqahtani, J. S., Alahamri, M. D., Alqahtani, A. S., Alamoudi, A. O., Alotaibi, N. Z., Ghazwani, A. A., Aldhahir, A. M., Alghamdi, S. M., Obaidan, A., & Alharbi, A. F. (2022). Early mobilization of mechanically ventilated ICU patients in Saudi Arabia: Results of an ICU-wide national survey. *Heart & Lung*, *56* .174-167 ,

Balachandran, A., Shivbalan, S., & Thangavelu, S. (2005). Chest physiotherapy in pediatric practice. *Indian pediatrics*, *42*(6), 559 .

Brown, J. K., Singh, K., Dumitru, R., Chan, E., & Kim, M. P. (2018). The benefits of enhanced recovery after surgery programs and their application in cardiothoracic surgery. *Methodist DeBakey cardiovascular journal*, *14*(2), 77 .

Cacau, L. d. A. P., Oliveira, G. U., Maynard, L. G., Araújo Filho, A. A. d., Silva Junior, W. M. d., Cerqueria Neto, M. L., Antoniolli, A .R., & Santana-Filho, V. J. (2013). The use of the virtual reality as intervention tool in the postoperative of cardiac surgery. *Brazilian journal of cardiovascular surgery*, *28*, 281-289 .

Cassina, T., Putzu, A., Santambrogio, L., Villa, M., & Licker, M .J. (2016). Hemodynamic challenge to early mobilization after cardiac surgery: A pilot study. *Annals of cardiac anaesthesia*, *19*(3), 425 .

Cusack, B., & Buggy, D. (2020). Anaesthesia, analgesia, and the surgical stress response. *BJA education*, *20*(9), 321 .

da Costa Torres, D., Dos Santos, P. M. R., Reis, H. J. L., Paisani, D. M., & Chiavegato, L. D. (2016). Effectiveness of an early mobilization program on functional capacity after coronary artery bypass surgery: A randomized controlled trial protocol. *SAGE open medicine*, *4*, 2050312116682256 .

Dehghani, A., Hajibagheri, A., Azizi-Fini, I., Atoof, F., & Mousavi, N. (2020). Effect of an early mobilisation programme on pain intensity after laparoscopic surgery: a randomised clinical trial. *BMJ Supportive & Palliative Care*, bmjspcare-2020-002618. https://doi.org/10.1136/bmjspcare-2020-002618

Esmealy, L., Allahbakhshian, A., Gholizadeh, L., Khalili, A. F., & Sarbakhsh, P. (2023). Effects of early mobilization on pulmonary parameters and complications post coronary artery bypass graft surgery. *Applied Nursing Research*, *69*, 151653. https://doi.org/https://doi.org/10.1016/j.apnr.2022.151653

Ferreira L, Tanaka K, Santos-Galduróz RF, Galduroz JCF: Respiratory training as strategy to prevent cognitive decline in aging: a randomized controlled trial. *Clinical Interventions in Aging* 2015, 10:593.

Greaves, D., Psaltis, P. J., Ross, T. J., Davis, D., Smith, A. E., Boord, M. S., & Keage, H. A. (2019). Cognitive outcomes following coronary artery bypass grafting: a systematic review and meta-analysis of 91,829 patients. *International journal of cardiology*, *289*, 43-49 .

Habib, S., Afridi, M. I., Saeed, A., Jan, A. F., & Amjad, N. (2014). Frequency and predictors of cognitive decline in patients undergoing coronary artery bypass graft surgery. *Journal of the College of Physicians and Surgeons Pakistan*, *24*(8), 543-549 .

Hardiman, S. C., Villan Villan, Y. F., Conway, J. M., Sheehan, K. J., & Sobolev, B. (2022). Factors affecting mortality after coronary bypass surgery: a scoping review. *Journal of cardiothoracic surgery*, *17*(1), 1-14 .

Harris, C. L., & Shahid, S. (2014). Physical therapy–driven quality improvement to promote early mobility in the intensive care unit. Baylor University Medical Center Proceedings ,

Hunter, A., Johnson, L., & Coustasse, A. (2020). Reduction of intensive care unit length of stay: the case of early mobilization. *The health care manager*, *39*(3), 109-116 .

Irman, V., & Darma, I. Y. (2020). The effect of early mobilization on pain intensity in patients post appendectomy .. Proceeding International Conference Syedza Saintika ,

Kanejima, Y., Shimogai, T., Kitamura, M., Ishihara, K., & Izawa, K. P. (2020). Effect of early mobilization on physical function in patients after cardiac surgery: a systematic review and meta-analysis. *International Journal of Environmental Research and Public Health*, *17*(19), 7091 .

Klypa, T., Antonov, I., & Vavakin, A. (2016). The cognitive status dynamic of cardiosurgical patients and the predictors of its disturbance. *Anesteziologiia i Reanimatologiia*, *61*(1), 18-23 .

Kotekar, N., Shenkar, A., & Nagaraj, R. (2018). Postoperative cognitive dysfunction–current preventive strategies. *Clinical interventions in aging*, *13*, 2267 .

Kress, J. P., & Hall, J. B. (2014). ICU-acquired weakness and recovery from critical illness. *New England Journal of Medicine*, *370*(17), 1626-1635 .

Le, A. M. M. G., Le, N. L. T. K. n., McE, E. B. d. S. P. K., & GÃ³mez, L. D. (2021). Benefits of early mobilization in postoperative cardiac surgery patients. *Biomedical Journal of Scientific & Technical Research*, *36*(2), 28391-28396 .

MacKenzie, E., Patel, B. K., Wolfe, K. S., Pohlman, A. S., Hall, J. B., & Kress, J. P. (2016). Long-term cognitive outcomes of mechanically ventilated patients in a randomized controlled trial of early mobilization. In *A25. Critical Care: Functional Outcomes In ICU Survivors* (pp. A1176-A1176). American Thoracic Society .

Mahesh, B., Choong, C. K., Goldsmith, K., Gerrard, C., Nashef ,S. A., & Vuylsteke, A. (2012). Prolonged stay in intensive care unit is a powerful predictor of adverse outcomes after cardiac operations. *The Annals of thoracic surgery*, *94*(1), 109-116 .

Marra, A., Ely, E. W., Pandharipande, P. P., & Patel, M. B. (2017 .(The ABCDEF bundle in critical care. *Critical care clinics*, *33*(2), 225-243 .

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. *Crit Care Med*, *36*(8), 2238-2243. https://doi.org/10.1097/CCM.0b013e318180b90e

Myles, P. S., Myles, D. B., Galagher, W., Boyd ,D., Chew, C., MacDonald, N., & Dennis, A. (2017). Measuring acute postoperative pain using the visual analog scale: the minimal clinically important difference and patient acceptable symptom state. *British Journal of Anaesthesia*, *118*(3), 424-429. https//:doi.org/https://doi.org/10.1093/bja/aew466

Nydahl, P., Spindelmann, E., Hermes, C., Kaltwasser, A., & Schaller, S. J. (2020). German network for early mobilization: impact for participants. *Heart & Lung*, *49*(3), 301-303 .

Ochroch, J., Usman, A., Kiefer ,J., Pulton, D., Shah, R., Grosh, T., Patel, S., Vernick, W., Gutsche, J. T., & Raiten, J. (2021). Reducing opioid use in patients undergoing cardiac surgery–preoperative, intraoperative, and critical care strategies. *Journal of cardiothoracic and vascular anesthesia*, *35*(7), 2155-2165 .

Pooria, A., Pourya, A., & Gheini, A. (2020). Postoperative complications associated with coronary artery bypass graft surgery and their therapeutic interventions. *Future Cardiology*, *16*(5), 481-496 .

Roberson, A. R., Starkweather, A., Grossman, C., Acevedo, E., & Salyer, J. (2018). Influence of muscle strength on early mobility in critically ill adult patients: systematic literature review. *Heart & Lung*, *47*(1), 1-9 .

Ronnebaum, J., Weir, J., & Hilsabeck, T. (2012). Earlier Mobilization Decreases the Length of Stay in the Intensive Care Unit. *Journal of Acute Care Physical Therapy*, *3*(2), 204-210 .

Seventina, H. (2020). Effect of early mobilization on the decrease in pain intensity among post cesarean section patients at Cirebon Hospital in 2019. 1st International Conference on Science, Health, Economics, Education and Technology (ICoSHEET 2019 ,(

Shirvani, F., Naji, S. A., Davari, E., & Sedighi, M. (2020). Early mobilization reduces delirium after coronary artery bypass graft surgery. *Asian Cardiovascular and Thoracic Annals 28*(9), 566-571. https://doi.org/10.1177/0218492320947230

Subramanian, M., Kozower, B. D., Brown, L. M., Khullar, O. V., & Fernandez, F. G. (2019). Patient-reported outcomes in cardiothoracic surgery. *The Annals of thoracic surgery*, *107*(1), 294-301 .

Tatari, F., Farnia, V., & Kazemi, F. (2011). Mini Mental State Examination (MMSE) in first episode of psychosis. *Iranian Journal of Psychiatry*, *6*(4), 158-160 .

Tatari F, Farnia V, Kazemi F: Mini Mental State Examination (MMSE) in first episode of psychosis. *Iranian Journal of Psychiatry* 2011, **6**(4):158-160.Totonchi, Z., Seifi, S., Chitsazan, M., Ghavidel ,A. A., Baazm, F., & Faritus, S. Z. (2014). Pain location and intensity during the first week following coronary artery bypass graft surgery. *Anesthesiology and pain medicine*, *4*(1 .(

Traub, J., Otto, M., Sell, R., Homola, G. A., Steinacker, P., Oeckl, P ,.Morbach, C., Frantz, S., Pham, M., & Störk, S. (2022). Serum glial fibrillary acidic protein indicates memory impairment in patients with chronic heart failure. *ESC heart failure*, *9*(4), 2626-2634 .

Wischmeyer, P. E., & San-Millan, I. (2015). Winning the war against ICU-acquired weakness: new innovations in nutrition and exercise physiology. *Critical Care*, *19*(3), 1-14 .

Zarrizi, M., Paryad, E., Khanghah, A. G., Leili, E. K., & Faghani, H. (2020). Predictors of length of stay in intensive care unit after coronary artery bypass grafting: development a risk scoring system. *Brazilian journal of cardiovascular surgery*, *36*, 57-63 .

Ziyaeifard, M., Khoo, F. G. B., Lotfian, S., Azarfarin, R., Aminnejad, R., Alikhani, R., & Moghadam, M. Y. (2018). Effects of early mobilization protocol on cognitive outcome after cardiac surgery. *Annals of Anesthesiology and Critical Care*, *3*(1), 1-8 .