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Effects of Early Mobilization Protocol on Cognitive Outcome after Cardiac Surgery

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Abstract

Background: This study aimed at determining the effects of implementation of “early mobilization protocol” on incidence of cognitive dysfunction after cardiac surgery.
Methods: In a randomized controlled trial, 80 adult patients, who had undergone elective cardiac surgery were randomly assigned to intervention (early mobilization protocol; n = 40) and control (routine physical therapy; n = 40) groups. Early mobilization was initiated from the first post-op morning and continued until discharge from the ICU. Cognitive dysfunction was assessed by the mini mental state examination (MMSE) questionnaire. The MMSE questionnaire was completed at three occasions for every patient: one day before surgery, second post-op day, and at the time of discharge from the intensive care unit (ICU).
Results: Preoperative cognitive status had no difference between the two groups (P = 0.310). Post-op cognitive dysfunction was significantly more commonly reported in the control group. The MMSE scores were higher in early mobilized patients compared to the control group on the first post-op day (median: 28; inter quartile range: 26 to 30 versus median: 25; IQR: 22 to 27; p = 0.001) and at the time of discharge from the ICU (median: 29; IQR: 28 to 30 versus median: 26; IQR: 25 to 28; p = 0.001). In multivariate analysis, duration of tracheal intubation and “early mobilization protocol” had significant effects on patients’ length of ICU stay.
Conclusions: Implementation of early mobilization protocol has positive effects on cognitive outcome and ICU stay after cardiac surgery.

Keywords: Cardiac Surgery, Early Mobilization, Cognitive Disorders

1. Background

Cardiac surgery is among the most critical and life-saving operations with potential complications as well as considerable socioeconomic burden. To provide appropriate care, a wide range of knowledge is necessary on possible preoperative, intraoperative, and postoperative complications. Among these complications is clinical neurologic complications, including postoperative cognitive disorders (POCD) (1).

Neurocognitive dysfunction after cardiac surgery can be observed in 30% to 70% of patients. Two major risk factors include increasing depth of anesthesia and intraoperative decline of cerebral oxygenation. Use of larger tidal volumes during mechanical ventilation, continued low cardiac output without timely intraoperative correction, and perioperative hyperglycemia are other important factors that may lead to postoperative neurologic complications in cardiac surgery patients (2). Preoperative cognitive reserve is a predictive element for the occurrence of POCD. There is evidence that shows patients with higher educational level have lower risk of POCD (3).

The higher incidence of POCD in cardiac surgeries is attributed to extended alterations in the brain function throughout the procedure compared to other non-cardiac surgeries (4). Decline in cognition has been attributed to brain cellular injury as demonstrated by elevated plasma Glial fibrillary acid protein (GFAP) concentrations (5), or particularly interleukin-6, and S-100β (6).

There is no single definitive treatment for POCD other than preventive measures; a multimodal approach is suggested, in which a major aspect is timely rehabilitation and early discharge of the patients (7). Early mobilization after surgical procedures has prominent benefits, among which are reduced length of hospital stay and morbidity rates (8). Early mobilization in critically ill patients can lead to less cognitive disorders, including delirium (9). In this study, the researchers aimed at evaluating the beneficial effects of early ambulation on occurrence of postoperative cognitive disorders, in cardiac surgery patients, for the first time in Iran.

2. Methods

2.1. Ethical Considerations

The study was reviewed and approved by the institutional review boards and the hospital ethics committee (RHC.AC.IR.REC.1396.46). All procedures and actions were performed in accordance with the ethical standards laid down in an appropriate version of the 2000 declaration of Helsinki (http://www.wma.net/e/policy/b3.htm). Thorough and detailed information on the study protocol were provided in both oral and written forms to all patients. All participants provided an informed written consent prior to participation, according to the Hospital Ethics Committee.

2.2. Study Design and Participants

In a randomized clinical trial, all adult patients, who had undergone cardiac surgery in an academic hospital located in a major referral center were recruited from March to September 2016. Cognitive assessment (validated Farsi version of the mini-mental state examination or MMSE) was performed in three sessions for all those, who met the inclusion criteria. Patients were randomly allocated to the intervention and control group without being aware of their group of assignment after surgery. This study included patients if they were between the ages of 20 to 70, had the ability to read and write, did not have emergent need for open heart surgery, and were cooperative (RASS between -2 and 2). Exclusion criteria were as follows: Inability to communicate, preexisting cognitive or psychological disorders, cardiac arrest during or after surgery, neurologic disturbances, and presence of severe visual/auditory dysfunction, or any contra-indications for early mobilization (including respiratory incompetence; need for FiO2 values more than 0.85 and PEEP equal to 15 cmH2o or more), acute myocardial ischemia, uncontrolled dysrhythmia, unstable blood pressure despite use of vasopressors, and presence of an open sternum. The early mobilization protocol (EMP) was initiated on the second post-op day by a research physician and a physiotherapist based on the clinical assessment, and was continued until discharge from the ICU. For controls, physiotherapy was performed only at bedside by means of vibration over chest, incentive spirometry, and encouraging the patient to cough; patients were not mobilized at all during their ICU stay.

2.3. Early Mobilization Protocol (EMP)

In the current study, patient assessment and implementation of the EMP were started on the second day after open heart surgery, although similar studies have initiated EMP as early as eight hours after ICU admission (10). For any patient, who met the inclusion criteria, sedation status (Figure 1) was evaluated by Richmond agitation-sedation scale (RASS). Details of different activity levels based on EMP protocol are as follows.

2.3.1. Level 1 Activity

At this level, the patient is totally dependent on assistance. Hence, inactive movements in the patient's range of motion (ROM) are applied twice daily ten times in each cycle, as well as head elevation over the bed ($\geq$ 30°) for 15 minutes and change of position for every two hours. In a patient with RASS between -2 and +2, who tolerates level 1 activity, level 2 could be started.

2.3.2. Level 2 Activity

At this level, the patient still needs help. Active movements in patient's ROM (twice daily, ten times in each cycle), head elevation over the bed ($\geq$ 45°) for 15 minutes, and maintaining the sitting position for 15 minutes on the bed are parts of this level of activity. If the patient tolerates level 2 activity, then the next level (level 3) could be started.

2.3.3. Level 3 Activity

At this level, the patient needs low to moderate level of assistance. Active movements in patient's ROM (twice daily; ten times in each cycle), head elevation over the bed ($\geq$ 45°) for 15 minutes, maintaining the sitting position for 15 minutes on the bed, and sitting at the edge of the bed hanging feet with the aid of a nurse for 15 minutes are parts of this level of activity. If the patient tolerates level 3 activity, then level 4 could be applied.

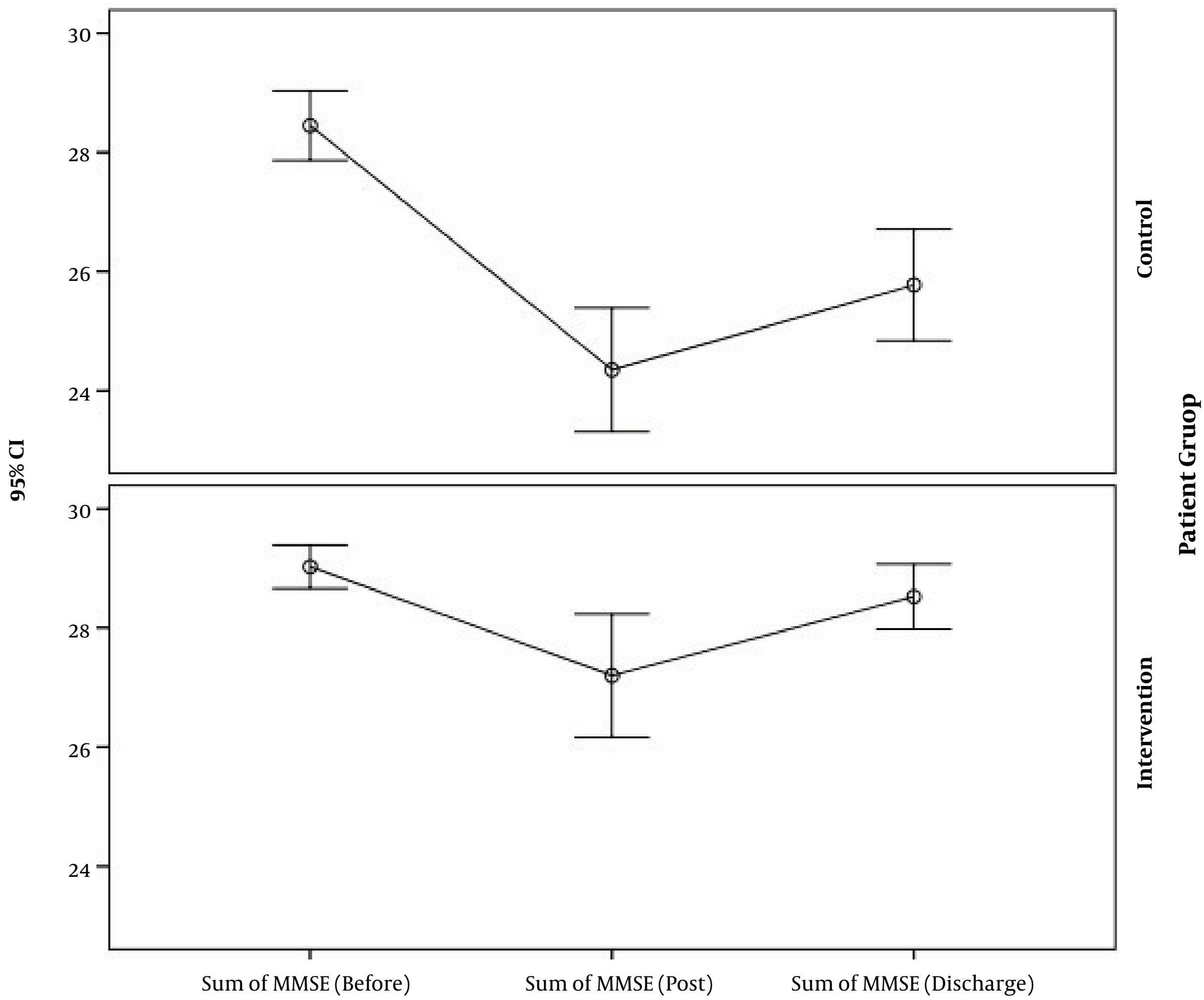

Figure 1. Comparing the status of cognitive impairment at three stages of measurement based on group of assignment (intervention vs. control)

2.3.4. Level 4 Activity

At this level, the patient requires minimal assistance and nurse supervision would suffice for activities. Active movements in patient's ROM (twice daily; ten times in each cycle), head elevation over the bed ($\geq$ 45°) for 15 minutes, maintaining the sitting position for 15 minutes on the bed, sitting at the edge of the bed and hanging feet with the aid of a nurse for 15 minutes, patient transport to the chair next to the bed by a nurse and restricted bedside walking or walking around the ward for stable patients, are parts of this level of activity.

2.4. Control Group

No experimental protocol was implemented for the control group, except for routine physiotherapy by a nurse physiotherapist.

2.5. Cognitive Assessment

The MMSE questionnaire was completed three times for patients in the intervention and control groups; a day before surgery, on the second postoperative day, and at the time of discharge from the ICU in both groups.

2.6. Data Analysis

Acquired data were entered in the statistical package for social sciences (IBM Inc. Version 16.0). For inferential statistics, Kolmogorov– Smirnov test was used to determine the normality of variables. According to the type of variable, suitable tests were defined. In inferential statistics, significance of relationship between demographic variables were studied in the intervention and control groups. Mann-Whitney U test was utilized to compare MMSE scores between the two groups. Friedman test was used to analyze the relationship between demographic variables and cognitive disorder at the time of discharge from the hospital. Multivariate analysis was implemented to check for confounding factors, such as type of surgery, duration of surgery, duration of cardiopulmonary pump, and cardiac ejection fraction. P values less than 0.05 were considered statistically significant.

3. Results

In total, 80 patients were recruited. All patients, who were candidates for cardiac surgery from March to September 2016 were assessed based on the inclusion criteria before and after surgery. For patients, who consented to participate, the MMSE questionnaires were completed.

3.1. Demographic and Clinical Characteristics

Mean age of the participants was 54.39 (SD or standard deviation: 14.60) and their mean body weight was 73.90 Kg (SD: 13.70). Sixty-five were males and 45% had elementary school education. Coronary heart disease was the underlying cause of surgery in 61.3% (valvular heart disease: 33.8%; congenital heart disease: 5%). In their medical history, 67.5% had diabetes, 47.3% had hypertension, and 17.5% had history of substance abuse. More than 55% had history of other surgeries and 38.8% had received inotropes after surgery. Other important laboratory and clinical variables for the participants are shown in Table 1.

Chi-square and Mann-Whitney U tests were performed to check for comparability of the patients in intervention and control groups at baseline. The two groups were comparable with regards to their age, gender, level of education, body weight, body temperature, hematocrit, history of hypertension, diabetes and substance abuse, history of past surgery, and underlying heart disease ($P > 0.05$). However, participants had significant differences in their history of post-op inotrope administration ($P = 0.001$) and left ventricular ejection fraction ($P = 0.013$).

3.2. The MMSE Scores

The mean score for all participants was reported as 28.74 at baseline (SD: 1.54; SE: 0.172) with no significant difference between intervention and control groups ($P = 0.318$). Patients had significantly higher scores on the second post-op day, and at the time of discharge from the ICU in the intervention group ($P < 0.001$). Presence and severity of cognitive impairment in the two groups are shown in Table 2 at three stages of measurement (Table 2). This research performed further analysis to compare the findings along with demographic, laboratory, and clinical characteristics of patients after discharge from the ICU (Table 3).

Figure 1 indicates changes in mean MMSE scores in both intervention and control groups. As shown, there was no significant relationship between preoperative cognitive impairment and assignment to the intervention or control group ($P > 0.05$). However, there was a significant relationship between cognitive impairment on the second post-op day and at the time of discharge from the ICU, and group of assignment ($P < 0.05$).

The components of the MMSE questionnaire were also measured at baseline, on the second post-op day, and at the time of discharge from the ICU in the intervention and control groups by Mann-Whitney U test. On the second post-op day, awareness of time, awareness of place, attention and calculation, recent memory, and lingual function scores were significantly higher in the intervention group ($P < 0.05$). Registration was also significantly better in the intervention group at the time of discharge from the ICU ($P = 0.041$).

3.3. Other Comparisons

Duration of intubation and ICU stay were both significantly higher in the control group ($P = 0.017$; $P \leq 0.001$). Thirty-four patients (85%) in the intervention group did not experience any cognitive impairment and only 15% (6 patients) had mild cognitive impairment at the time of discharge. Prevalence of moderate, mild, and no cognitive impairment was reported to be 5% (two patients), 50% (20 patients), and 45% (18 patients), respectively. With the use of linear regression test, it appeared that left ventricular ejection fraction and inotropic agent administration had no beneficial effects on duration of ICU stay. However, decreased period of intubation and implementation of EMP could lead to diminished ICU stay (Table 4).

Table 1. Important Laboratory and Clinical Characteristics of Participants at Baseline, During and After Cardiac Surgery

Variables	Frequency	Change Range	Minimum	Maximum	Average	Standard Error	Standard Deviation
Blood pressure (systolic)	80	62	90	152	121.34	1.84	16.46
Blood pressure (diastolic)	80	32	57	89	72.43	0.74	6.65
Cardiopulmonary bypass time (min)	80	187	38	225	86.65	4.10	36.69
Aortic cross-clamping time (min)	80	140	20	160	51.70	3.240	28.98
Body temperature (°C)	80	9	27	36	31.81	0.177	1.58
Hematocrit (%)	80	27	19	46	28.71	0.542	4.848
Left ventricular ejection fraction (%)	80	40	20	60	45	0.001	8.949
Duration of intubation (hours)	80	34	7	41	15	0.6069	5.4286
Length of ICU stay (hours)	80	76	20	96	48	1.3423	12.0062

Table 2. Comparing the Presence and Severity of Cognitive Impairment in Intervention and Control Groups at Three Stages of Measurement

Variables	Control Group (n=40)	Intervention Group (n=40)	Test	Significance (P-Value)[a]
Preoperative cognitive impairment			Friedman	0.139
None	34 (85%)	38 (95%)		
Mild	6 (15%)	2 (5%)		
Moderate	-	-		
Cognitive impairment on 2nd post-op day			Friedman	< 0.001
None	11 (28%)	28 (70%)		
Mild	23 (58%)	11 (28%)		
Moderate	6 (15%)	1 (3%)		
Cognitive impairment at the time of discharge from ICU			Friedman	< 0.001
None	18 (45%)	34 (85%)		
Mild	20 (50%)	6 (15%)		
Moderate	2 (5%)	0 (0%)		

[a] Level of significance < 0.05.

4. Discussion

Post-operative cognitive dysfunction is a known clinical phenomenon after cardiac surgeries, however, there is not enough evidence about the incidence, predisposing factors, and long term prognosis. In the perioperative period, cerebral hypoperfusion, systemic inflammatory responses, use of cardiopulmonary bypass circuit, and hyperthermia are potential perpetuating factors (11).

At bedside, POCD can be defined as reduction in any domain of cognition, following surgery, specially thinking and memory, without significant alterations in the level of consciousness (confusion). This disabling complication can occur in up to 70% of patients in the first post-op week, yet the incidence reduces in upcoming days following surgery. The diagnosis of POCD early in the postoperative period is difficult and sometimes challenging. An important practical point is to differentiate POCD from postoperative delirium. Cognitive dysfunction has unwanted impacts on social and personal life of the patient, and may lead to dependence in the long term. Additionally, POCD can increase mortality rates in hospitalized patients (11). Hence, understanding potential preventive measures can help patients have a normal life after cardiac surgery.

Early mobilization after cardiac surgery can lead to shorter hospital stay and fewer postoperative complications. There is no significant difference between various methods of mobilization, considering the major aim that is to avoid long-term stay in bed after surgery (12). However, "patient safety" is a concern with the most important aspect being the hemodynamic status of the patient. It has been documented that early mobilization in this group of patients wouldn't adversely affect hemodynamic values.

Table 3. Comparing the Presence and Severity of Cognitive Impairment along Demographic, Laboratory, and Clinical Characteristics of the Participants after Discharge from the ICU

Variables	No Cognitive Disorder	Mild Cognitive Disorder	Moderate Cognitive Disorder	Test	Significance (P-Value)
Age[a] (y)	58 (43 - 63)	62 (53 - 70)	-	Kruskal-Wallis	0.117[b]
Gender[c]					
Female	19 (37)	9 (34)	0 (0)	Chi-square	0.568
Male	33 (63)	17 (66)	2 (100)	Kruskal-Wallis	0.689
Weight[a] (kg)	71 (61 - 83)	75 (66 - 85)	-	Kruskal-Wallis	0.165
Level of education[c]				Kruskal-Wallis	0.001
Elementary	16 (30.8)	18 (69.2)	2 (100)		
Secondary	25 (48.1)	5 (30.8)	0 (0)		
Higher	11 (21.2)	0 (0)	0 (0)		
Types of heart disease[c]				Chi-square	0.396
Valvular	16 (31)	11 (42)	0 (0)		
Coronary	32 (62)	15 (58)	2 (100)		
Congenital	4 (8)	0 (0)	0 (0)		
History of diabetes[c]	13 (25)	12 (46)	1 (50)	Chi-square	0.148
History of substance use[c]	8 (15)	5 (19)	1 (50)	Chi-square	0.432
History of surgery[c]	31 (60)	14 (54)	0 (0)	Chi-square	0.238
History of hypertension[c]	25 (48)	13 (50)	0 (0)	Chi-square	0.390
Postoperative administration of inotropes[c]	17 (33)	14 (54)	0 (0)	Chi-square	0.102
Cardiopulmonary bypass time[a] (m)	85				
(57 - 114)	73				
(60 - 95)	-	Kruskal-Wallis	0.417		
Aortic cross - clamping time[a] (min)	45				
(30 - 63)	35				
(31 - 75)	-	Kruskal-Wallis	0.879		
Body temperature[a] (°C)	32				
(31 - 32)	32				
(32 - 33)	-	Kruskal-Wallis	0.098		
Hematocrit[a] (%)	29				
(25 - 32)	26				
(25 - 29)	-	Kruskal-Wallis	0.175		
Duration of intubation[a] (hr)	13				
(10 - 17)	17				
(15 - 21)	12				
(7.5 - 12.5)	Kruskal-Wallis	0.005			

[a] Mean (minimum - maximum).
[b] Level of significance < 0.05.
[c] Frequency represented as No. (%).

Table 4. Clinical Factors That May Have Contributed to Longer ICU Stay

Variable	Unstandardized Coefficients		Standardized Coefficients	P-Value	Lower Limit	Upper Limit
	Standard Error	Beta				
Left ventricular ejection fraction (%)	80	0.14	0.09	0.3	-0.16	0.4
Duration of intubation (hours)	80	0.2	0.23	0.02	0.05	0.9
Postoperative administration of inotropes	80	2.7	0.17	0.12	-1.1	9.6
Implementation of early mobilization protocol	80	2.7	-0.26	0.02	-11.8	-0.9

Additionally, mobilization of a patient in an intensive care setting can minimize probable hazards by routine monitoring that is commonly available (13, 14).

Coexisting diseases in cardiac surgery patients is another concern. Diseases, such as diabetes mellitus or hypertension can influence the cognitive ability of a patient. In diabetic patients (for example) reduced gray matter in the cortico-striato-limbic networks can affect cognition (15). Hypertension can lead to reduced cognitive function by stiffening of arteries and compromising blood flow. Therefore, use of antihypertensive medications, such as calcium channel blockers and angiotensin receptor blockers, are associated with a decreased risk of cognitive impairment in hypertensive patients (16, 17).

Type of cardiac procedure is another contributing factor. For example, in young patients, who are going to have a cardiac valve repair or replacement, exposure of cardiac chambers to the room air can predispose patients to air emboli that can be a risk factor for post-op cognitive impairment (18).

The current findings showed that early ambulation can lead to decreased need for post-op inotropic agents. Duration of intubation and length of ICU stay were also significantly reduced by implementation of EMP. Freeman et al. showed that fast-track cardiac care is a proven method for reducing time to extubation and ICU length of stay, however, this method wouldn't lead to shorter hospital stay (19). Early extubation per se can also lead to better mental outcome in cardiac surgery patients (20). Therefore, shortening of intubation time after cardiac surgery could be an independent mechanism for less post-op cognitive impairment; as it is true for shorter duration of ICU stay.

Hughes et al. showed that baseline educational level was an important contributing factor in developing cognitive impairment after non-cardiac surgeries (21). Similarly, the current findings indicated that cognitive impairment was more common in less educated patients. Comparison of the components of the MMSE questionnaire between the two groups showed that implementation of EMP could lead to better mental outcome in cardiac surgery patients. This study showed that implementation of EMP in cardiac surgery patients can lead to decreased cognitive impairment one day following surgery and after discharge from the ICU. Seventy-three percent of patients in the control group had mild to moderate cognitive dysfunction a day after surgery; this was reduced to 55% after discharge from the ICU. In the intervention group, these figures were 31% and 15%, respectively.

4.1. Limitations

The sensitivity of the MMSE questionnaire is low in detection of cases of mild dementia and leads to false negative diagnoses in people with higher education. In addition, low literacy may result in false positive findings. However, the benefits outright the limitations and the current researchers decided to utilize MMSE as their main study tool to assess cognition.

4.2. Conclusion

In conclusion, EMP can be part of enhanced recovery after surgery (ERAS) protocols that are useful in a variety of surgical procedures. Application of ERAS protocols in cardiac surgery patients has beneficial effects on patients' outcome, especially in their cognitive function. The current researchers propose that EMP can be a practical and effective protocol for all centers that comply with ERAS (22). Progressive early mobility for patients on mechanical circulatory support (MCS) devices is known as the right thing to do (23). Thus, EMP could be implemented for patients with mechanical circulatory support devices as well.

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