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Prevalence and Predisposing Factors for Cognitive Dysfunction Following Adult Cardiac Surgery

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Abstract

Background: One of the adverse effects following cardiac surgery is cognitive dysfunction. The prevalence of cognitive dysfunction after heart surgery is reportedly 30% - 80%.

Objective: The purpose of this study was to evaluate the prevalence and risk factors of cognitive dysfunction in the ICU after heart surgery.

Methods: In this observational study, 99 adult patients who underwent elective cardiac surgery (valve and coronary) in a tertiary university hospital were examined. The cognitive state of the patients in the ICU 2 or 3 days after the operation was assessed using the MMSE scale. Perioperative predisposing factors were simultaneously considered.

Results: The results showed that the majority of the patients (55.5%) had no cognitive impairment, while 39.4% had mild cognitive impairment and 5.1% had moderate cognitive impairment. Cognitive dysfunction had a significant relationship with the following factors: age (P = 0.11), cardiopulmonary bypass time (P = 0.002), aortic cross-clamp time (P = 0.002), and literacy (P = 0.019). The results also showed that cognitive dysfunction had no significant relationship with sex, previous history of surgery, preoperative and postoperative hemoglobin, blood glucose, diabetes, type of operation, and duration of operation.

Conclusion: The results of this study showed that 39.4% of our patients had mild cognitive impairment and 5.1% experienced moderate cognitive impairment following cardiac surgery. Significant relationships between cognitive dysfunction and age, education level, cardiopulmonary bypass time, and aortic clamp time were seen. In the logistic regression analysis, only age was related to cognitive impairment.

Keywords: Cognitive Dysfunction, Cardiac Surgery, Risk Factors

1. Background

One of the adverse effects following cardiac surgery is cognitive dysfunction. Cognitive dysfunction comprises different levels, namely mild, moderate, and severe. Mild cognitive dysfunction is a slight decrease in recognition or executive actions with partial defects that may appear in various forms, which are apparent through objective evidence. For example, patients may get lost when going to an unfamiliar place. Their colleagues may notice a decrease in performance in detailed jobs. Patients may also have difficulty finding words and remembering the names of people. Concentration defects, which have been identified in clinical trials, may include the tendency to forget what has just been said and to repeat words (1-6). Moderate cognitive dysfunction is the state of slowly regaining consciousness after cardiac surgery, which can continue for several days. These patients wake up from anesthesia later and are often restless. Recovery occurs during the first week after surgery (1, 7-10). The prevalence of cognitive dysfunction after heart surgery is reportedly 30% - 80% (8). Severe cognitive disorders include delirium, dementia, and Alzheimer's disease. Delirium after surgical procedures is the most serious and most severe cognitive disorder, and can be associated with significant morbidity and mortality. The diagnosis of cognitive dysfunction is mostly limited to reactions that occur in the first 2 to 5 days after surgery (11-14).

Several factors affect the incidence of cognitive dysfunction. For example, patients undergoing heart surgery are at high risk for cognitive dysfunction. Age is also one of the main causes of cognitive dysfunction. Generally, age, comorbid diseases (such as thyroid disease, diabetes, hyperlipidemia, and hypertension), operation history, history of drug consumption, time of intubation, type of operation (valve replacement or coronary surgery), types of drugs for anesthesia, electrolyte disturbances (blood urea nitrogen, creatinine), inotrope drug consumption before and after surgery, use of intra-aortic balloons after surgery, and hypoxemia comprise the risk factors for cognitive dysfunction (1, 7, 15-23).

Patients undergoing cardiac surgery are at high risk for cognitive and functional defects. Postoperative cognitive dysfunction is associated with higher medical costs, longer hospital stays, a greater likelihood of referral to long-term care facility centers, inappropriate improvement, and death (3, 5, 6, 10, 24, 25). As a result, early diagnosis can decrease the duration of hospitalization and ICU stay, reduce morbidity and mortality rates, minimize the risk of infection, and lower costs.

2. Objectives

Today, the attention of researchers investigating the prevention and treatment of cognitive dysfunction has focused on the identification of risk factors. Prevention should take place on two levels: primary prevention (i.e., the reduction of risk factors) and secondary prevention (i.e., the early diagnosis of cognitive dysfunction). Because nurses are in frequent contact with patients, they can play an essential role in the prevention, diagnosis, and treatment of cognitive dysfunction. The aim in this study was therefore to examine the prevalence and risk factors of cognitive dysfunction in the ICU after heart surgery.

3. Methods

This observational study, which was carried out in 2015, aimed to determine the prevalence and risk factors of cognitive dysfunction before and after cardiac surgery in the ICU in Rajaie cardiovascular, medical and research center (Tehran, Iran). After obtaining institutional ethical approval and patient consent, patients were recruited for the study according to the inclusion criteria. The patients' mental state was assessed using the mini-mental state examination (MMSE) questionnaire.

3.1. Patients

According to the study of Xu et al. (8), the incidence of cognitive impairment after surgery is 33% - 83 %. We considered a confidence interval of 95% (50% - 60 %) and used online software (www.surveysystem.com/sscalc.htm) to calculate the sample size, which was determined to be 96. The final number of patients enrolled in our study was 99. The inclusion criteria were: adult patients aged 18 - 70 years with left ventricular ejection fraction > 30%who underwent valve repair or replacement and coronary artery bypass grafting, elective operation, no history of cognitive disorders or dysarthria, and no intubation before surgery. The exclusion criteria were cardiac arrest during or after surgery, stroke or coma in the postoperative period, and prolonged (> 24 hours) intubation.

We recorded the patients' demographic and risk factors data and used the MMSE questionnaire to assess the cognitive status of the patients. The MMSE questionnaire consisted of 6 parts and 17 questions, with a total of 30 scores. The different fields of cognitive function included orientation, registration, attention and calculation, recent memory, language functions, and spatial thinking. As a rule, the score for mild cognitive dysfunction is 20 - 24, moderate cognitive dysfunction is 11 - 19, and severe cognitive dysfunction is 0 - 10. The Persian translation of the MMSE questionnaire was validated and used by Sayedan et al. (26) in 2009.

3.2. Statistical analyses

The data were analyzed using statistical software SPSS Version 17.0 for Windows (SPSS IBM Inc. Chicago, IL). The K-S test was done on the interval data, and they were found to be normally distributed. The differences between the groups (no cognitive dysfunction, mild dysfunction, and moderate dysfunction) for the categorical variables were analyzed using a chi-squared or Fischer's exact test. The continuous data were compared by ANOVA and are expressed as mean $\pm$ SD. A $P \leq 0.05$ was considered statistically significant.

4. Results

Based on the inclusion criteria, 99 patients were enrolled in and completed the study. Their demographic data are described in Table 1. Although the frequency of cognitive dysfunction after cardiac surgery in this study was 44.5 %, the patients did not experience severe cognitive dysfunction in the postoperative period. The distribution of the severity of cognitive dysfunction after cardiac surgery is presented in Table 2. We divided our patients into three subgroups: no cognitive dysfunction (n = 55), mild cognitive dysfunction (n = 39), and moderate cognitive dysfunction (n = 5). The demographic characteristics and risk factors of the patients in the three subgroups are summarized in Table 3

ANOVA was used to determine the relationship between cognitive dysfunction and the patients' quantitative characteristics. The results of the variance analysis showed no significant differences between hemoglobin levels, blood pressure and blood sugar before and after surgery, and duration of surgery among the subgroups.

Table 1. Demographic Data of the Patients

Variable	Frequency (%)
Age, y	
Sex	
Male	41 (41.4)
Female	58 (58.6)
Education Level	
> High school	64 (64.6)
≤ High school	35 (35.4)
Type of surgery	
Vascular	47 (47.5)
Coronary	52 (52.5)
History of surgery	
Yes	29 (29.3)
Diabetes	
Yes	20 (20.2)
Hypertension	
Yes	46 (46.5)

Table 2. Distribution of the Severity and Frequency of Cognitive Dysfunction after Cardiac Surgery

Cognitive Dysfunction	Frequency (%)
No cognitive dysfunction	55 (55.5)
Mild cognitive dysfunction	39 (39.4)
Moderate cognitive dysfunction	5 (5.1)
Total	99 (100)

The results of this study also showed significant differences between the severity of the cognitive dysfunction and age (P = 0.011), literacy (P = 0.019), cardiopulmonary bypass (CPB) time (P = 0.002), and aortic clamp time (P = 0.001) (Table 4).

The results of this study indicated that the only factors that had a significant relationship with cognitive dysfunction were education level, age, aortic clamp time, and CPB time. However, in the logistic regression analysis, only age was significantly related to the impairment of cognitive status (Table 5).

5. Discussion

Our study had two objectives. In relation to the primary aim of the study, namely the frequency of cognitive dysfunction after cardiac surgery, the results showed that the majority of subjects in this study (55.5%) did not have cognitive dysfunction. Nevertheless, 39.4 % had mild cognitive dysfunction and 5.1 % had moderate cognitive dysfunction. It should be noted that none of the studied patients had severe cognitive dysfunction. Several studies about the incidence of cognitive dysfunction and delirium in Iran and other countries following surgery have been conducted. In the study by Xu et al. (8) in 2012 in China, the incidence of cognitive dysfunction was reportedly 33% - 83%. A cohort study that was carried out by Saczynski et al. (2012) in England showed that 46% of patients had postoperative delirium (12). The incidence of this cognitive disorder at 6 months after surgery was 40%, and 12 months after surgery, it was 30%. In a study conducted in Denmark by Funder et al. (4) (2009), the incidence of cognitive disorders after heart surgery was 30% - 80% less than one week after surgery, and 10% - 60% when measured 6 months after surgery. In a study carried out by the Saczynski et al. (12) in 2011, the incidence of cognitive disorders was 50% - 70% after surgery. It should be noted that in all the studies, the MMSE questionnaire was used to determine the incidence of cognitive impairment.

In relation to the secondary aim of this study, which was to determine the risk factors of cognitive dysfunction after cardiac surgery, we found that not only does cognitive dysfunction after cardiac surgery have a significant relationship with drug consumption, but those patients who had not used drugs had less severe cognitive dysfunction. With respect to the relationship between education level and cognitive dysfunction, the chi-square test results showed that cognitive dysfunction was significantly associated with level of education (P = 0.019): the patients who had a higher education level had a lower severity of cognitive impairment after surgery. This finding is consistent the results of the studies by Saczynski et al. and Funder et al. (4, 12).

We found no significant association between sex and cognitive dysfunction (P = 0.483), although Funder et al. showed that the incidence of cognitive disorders was higher in men than women (4). Conversely, in Saczynski et al.'s study (12), the incidence was higher in women. The results of our study showed a significant relationship between age and cognitive dysfunction (P = 0.011). This finding corresponds with the results of several previous studies, such as those by Xu et al. (2013) and Hudetz et al. (2011), which found evidence that cognitive dysfunction after surgery increases with age (8, 10).

In terms of the relationship between cognitive dysfunction and the type of surgery, the results of our study did not correspond with those of Hudetz et al. (10). In their study, a significant relationship was found between the incidence of delirium in patients with and without CABG

Table 3. Patients' Characteristics, Risk Factors, and Type of Surgery

Variable	No cognitive Dysfunction n = 55	Mild Cognitive Dysfunction n = 39	Moderate Cognitive Dysfunction n = 5	P Value
Sex				0.83
Male	15 (36.6)	25 (61)	1 (2.4)	
Female	24 (41.4)	30 (51.7)	4 (6.9)	
Type of surgery				0.75
Valvular	21 (44.7)	24 (51.1)	2 (4.3)	
Coronary	18 (34.8)	31 (59.6)	3 (5.8)	
History of surgery				0.78
Yes	14 (48.3)	13 (44.8)	2 (6.9)	
Inotrope drug use				0.56
Yes	25 (44.6)	30 (53.6)	1 (1.8)	
Education level				0.19
> High school	22 (34.4)	41 (58.1)	1 (1.6)	
≤ High school	17 (48.6)	14 (40)	4 (11.4)	
Diabetes				0.19
Yes	11 (55)	9 (45)	0	
Hypertension				0.83
Yes	22 (47.8)	20 (43.5)	4 (8.7)	

surgery (P = 0.01), but in this study, no relationship was reported (P = 0.575). Our results on the relationship between aorta clamp time and cognitive dysfunction were similar to those of Xu et al. and Hudetz et al. (8, 10).

In our study, there was a significant difference between the mean aortic clamp time and the patients without cognitive dysfunction, those with mild cognitive dysfunction, and those with moderate cognitive dysfunction, although those with moderate cognitive dysfunction had a higher mean aortic clamping time than the other groups. It can therefore be concluded that the risk of cognitive dysfunction increases concomitantly with an increase in aortic clamp time (8, 10).

The results of this study indicated a significant difference in CPB time between patients without cognitive dysfunction, those with mild cognitive dysfunction, and those with moderate cognitive dysfunction. Patients with moderate cognitive dysfunction had higher CPB times than the other two groups. It can therefore be concluded that cognitive dysfunction increases with increasing CPB time. This finding corresponds with the results of Xu et al. (8). Our results can be generalized to adult patients who undergo elective cardiac valve or coronary bypass surgery.

5.1. Conclusions

To determine the prevalence and risk factors of cognitive dysfunction after heart surgery, we assessed 99 patients who underwent cardiac surgery with admission to ICU. Our results showed that there was no significant relationship between cognitive dysfunction and gender, history of surgery, hemoglobin value before and after surgery, blood pressure before and after surgery, blood sugar before and after surgery, diabetes mellitus, and type and duration of surgery. However, cognitive dysfunction had a significant relationship with age, education level, CPB, and aortic clamp time. In the logistic regression analysis, only age was significantly related to impaired cognitive function.

5.2. Limitations

This was a single-center study and did not include emergent or complex cardiac procedures. Additionally, we only evaluated the early cognitive status of the patients; therefore, mid- and long-term follow-ups are needed for a better assessment of late cognitive impairment in this patient population.

Table 4. Relationship Between the Severity of the Cognitive Dysfunction and the Clinical Variables of the Patients

Variable	No Cognitive Dysfunction n = 55	Mild Cognitive Dysfunction n = 39	Moderate Cognitive Dysfunction n = 5	P Value
Age, y	50.0 ± 14.9	57.3 ± 9.8	60.2 ± 9.7	0.001
Sex (M/F)	25/30	15/24	1/4	0.830
Weight, kg	67.7 ± 16.5	71.2 ± 9.6	72.4 ± 16.9	0.450
CPB time, min	81.8 ± 33.7	93.8 ± 0.3	139.2 ± 38.8	0.001
Aortic clamp time, min	52.5 ± 23.6	61.3 ± 23.8	99.0 ± 22.5	0.001
Duration of surgery, h	4.31 ± 1.15	4.33 ± 1.13	5.20 ± 1.78	0.269
Preoperative systolic blood pressure, mmHg	113.6 ± 14.2	113.7 ± 17.4	116.0 ± 11.4	0.948
Postoperative systolic blood pressure, mmHg	116.9 ± 16.4	116.0 ± 19.2	120.4 ± 5.8	0.859
Preoperative diastolic blood pressure, mmHg	71.1 ± 7.6	70.8 ± 11.3	72.0 ± 13.0	0.957
Postoperative diastolic blood pressure mmHg	69.9 ± 9.1	69.3 ± 12.3	74.0 ± 10.1	0.649
Preoperative hemoglobin, g/dL	12.78 ± 1.97	13.54 ± 2.01	13.80± 3.27	0.168
Postoperative hemoglobin, g/dL	10.27 ± 1.17	10.44 ± 1.66	8.80 ± 1.64	0.056
Preoperative blood sugar, mg/dL	124.9 ± 7.9	138.4 ± 57.2	126.6 ± 42.5	0.459
Postoperative blood sugar, mg/dL	174.4 ± 54.3	179.9 ± 63.0	203.8 ± 29.6	0.531
Duration of intubation, h	2.02 ± 0.14	2.05 ± 0.22	2.0 ± 0.1	0.610

Table 5. Logistic Regression Analysis

Variable	Estimate	Coefficient of Regression	Degrees of Freedom	Significance Level
Age	0.014	2.21	1	0.137
CPB* time	0.058	4.87	1	0.027
Aortic clamp time	0.024	3.15	1	0.076
Educational level	0.502	0.904	1	0.342

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Footnote

Authors' Contribution: Mohsen Ziyaeifard: conducted the study; Mehri Amiri and Azin Alizadehasl: administration, and technical and scientific revision of the paper; Habiballah Rezaei and Seyed Hamidreza Faiz: literature search and clinical analysis; Touraj Babaee: data interpretation and clinical analysis; Amir Reza Golbargian: data interpretation, critical revision of the paper, data collection, and manuscript preparation.

References

1. Rudolph JL, Schreiber KA, Culley DJ, McGlinchey RE, Crosby G, Levitsky S, et al. Measurement of post-operative cognitive dysfunction after cardiac surgery: a systematic review. *Acta Anaesthesiol Scand.* 2010;**54**(6):663–77. doi: 10.1111/j.1399-6576.2010.02236.x. [PubMed: 20397979].
2. Delphin E, Jackson D, Gubenko Y, Botea A, Esrig B, Fritz W, et al. Sevoflurane provides earlier tracheal extubation and assessment of cognitive recovery than isoflurane in patients undergoing off-pump coronary artery bypass surgery. *J Cardiothorac Vasc Anesth.* 2007;**21**(5):690–5. doi: 10.1053/j.jvca.2006.12.008. [PubMed: 17905275].
3. van Dijk D, Spoor M, Hijman R, Nathoe HM, Borst C, Jansen EW, et al. Cognitive and cardiac outcomes 5 years after off-pump vs on-pump coronary artery bypass graft surgery. *JAMA.* 2007;**297**(7):701–8. doi: 10.1001/jama.297.7.701. [PubMed: 17312289].

4. Funder KS, Steinmetz J, Rasmussen LS. Anaesthesia for the patient with dementia undergoing outpatient surgery. *Curr Opin Anaesthesiol.* 2009;**22**(6):712–7. doi: 10.1097/ACO.0b013e328331a4eb. [PubMed: 19734784].
5. Liu YH, Wang DX, Li LH, Wu XM, Shan GJ, Su Y, et al. The effects of cardiopulmonary bypass on the number of cerebral microemboli and the incidence of cognitive dysfunction after coronary artery bypass graft surgery. *Anesth Analg.* 2009;**109**(4):1013–22. doi: 10.1213/ane.0b013e3181aed2bb. [PubMed: 19762724].
6. Siepe M, Pfeiffer T, Gieringer A, Zemann S, Benk C, Schlensak C, et al. Increased systemic perfusion pressure during cardiopulmonary bypass is associated with less early postoperative cognitive dysfunction and delirium. *Eur J Cardiothorac Surg.* 2011;**40**(1):200–7. doi: 10.1016/j.ejcts.2010.11.024. [PubMed: 21168339].
7. Gerriets T, Schwarz N, Sammer G, Baehr J, Stolz E, Kaps M, et al. Protecting the brain from gaseous and solid micro-emboli during coronary artery bypass grafting: a randomized controlled trial. *Eur Heart J.* 2010;**31**(3):360–8. doi: 10.1093/eurheartj/ehp178. [PubMed: 19541675].
8. Xu T, Bo L, Wang J, Zhao Z, Xu Z, Deng X, et al. Risk factors for early postoperative cognitive dysfunction after non-coronary bypass surgery in Chinese population. *J Cardiothorac Surg.* 2013;**8**:204. doi: 10.1186/1749-8090-8-204. [PubMed: 24175992].
9. Anastasiadis K, Argiriadou H, Kosmidis MH, Megari K, Antonitsis P, Thomaidou E. Neurocognitive outcome after coronary artery bypass surgery using minimal versus conventional extracorporeal circulation: a randomised controlled pilot study. *Heart.* 2011;**97**:1082–8.
10. Hudetz JA, Iqbal Z, Gandhi SD, Patterson KM, Byrne AJ, Pagel PS. Postoperative delirium and short-term cognitive dysfunction occur more frequently in patients undergoing valve surgery with or without coronary artery bypass graft surgery compared with coronary artery bypass graft surgery alone: results of a pilot study. *J Cardiothorac Vasc Anesth.* 2011;**25**(5):811–6. doi: 10.1053/j.jvca.2010.05.003. [PubMed: 20655248].
11. Gao L, Taha R, Gauvin D, Othmen LB, Wang Y, Blaise G. Postoperative cognitive dysfunction after cardiac surgery. *Chest.* 2005;**128**(5):3664–70. doi: 10.1378/chest.128.5.3664. [PubMed: 16304328].
12. Saczynski JS, Marcantonio ER, Quach L, Fong TG, Gross A, Inouye SK, et al. Cognitive trajectories after postoperative delirium. *N Engl J Med.* 2012;**367**(1):30–9. doi: 10.1056/NEJMoa1112923. [PubMed: 22762316].
13. de Tournay-Jette E, Dupuis G, Bherer L, Deschamps A, Cartier R, Denault A. The relationship between cerebral oxygen saturation changes and postoperative cognitive dysfunction in elderly patients after coronary artery bypass graft surgery. *J Cardiothorac Vasc Anesth.* 2011;**25**(1):95–104. doi: 10.1053/j.jvca.2010.03.019. [PubMed: 20650659].
14. Grape S, Ravussin P, Rossi A, Kern C, Steiner L. Postoperative cognitive dysfunction. *Trends Anaesthesia Crit Care.* 2012;**2**(3):98–103.
15. Donndorf P, Kuhn F, Vollmar B, Rosner J, Liebold A, Gierer P, et al. Comparing microvascular alterations during minimal extracorporeal circulation and conventional cardiopulmonary bypass in coronary artery bypass graft surgery: a prospective, randomized study. *J Thorac Cardiovasc Surg.* 2012;**144**(3):677–83. doi: 10.1016/j.jtcvs.2012.05.037. [PubMed: 22698563].
16. Van Harten A, Scheeren T, Absalom A. A review of postoperative cognitive dysfunction and neuroinflammation associated with cardiac surgery and anaesthesia. *Anaesthesia.* 2012;**67**(3):280–93.
17. Zhang H, Lu Y, Liu M, Zou Z, Wang L, Xu FY, et al. Strategies for prevention of postoperative delirium: a systematic review and meta-analysis of randomized trials. *Crit Care.* 2013;**17**(2):47. doi: 10.1186/cc12566. [PubMed: 23506796].
18. Newman S, Stygall J, Hirani S, Shaefi S, Maze M. Postoperative Cognitive Dysfunction after Noncardiac SurgeryA Systematic Review. *J Am Soci Anesthesiol.* 2007;**106**(3):572–90.
19. Gottesman RF, Grega MA, Bailey MM, Pham LD, Zeger SL, Baumgartner WA, et al. Delirium after coronary artery bypass graft surgery and late mortality. *Ann Neurol.* 2010;**67**(3):338–44. doi: 10.1002/ana.21899. [PubMed: 20373345].
20. Suwa M, Ito T. Correlation between cognitive impairment and left ventricular diastolic dysfunction in patients with cardiovascular diseases. *Int J Cardiol.* 2009;**136**(3):351–4. doi: 10.1016/j.ijcard.2008.04.099. [PubMed: 18684536].
21. Selnes OA, Gottesman RF, Grega MA, Baumgartner WA, Zeger SL, McKhann GM. Cognitive and neurologic outcomes after coronary-artery bypass surgery. *N Engl J Med.* 2012;**366**(3):250–7. doi: 10.1056/NEJMra1100109. [PubMed: 22256807].
22. van Harten AE, Scheeren TW, Absalom AR. A review of postoperative cognitive dysfunction and neuroinflammation associated with cardiac surgery and anaesthesia. *Anaesthesia.* 2012;**67**(3):280–93. doi: 10.1111/j.1365-2044.2011.07008.x. [PubMed: 22321085].
23. Vogels RL, Scheltens P, Schroeder-Tanka JM, Weinstein HC. Cognitive impairment in heart failure: a systematic review of the literature. *Eur J Heart Fail.* 2007;**9**(5):440–9. doi: 10.1016/j.ejheart.2006.11.001. [PubMed: 17174152].
24. Farhoudi M, Parvizi R, Bilehjani E, Tarzamni MK, Mehrvar K, Safaiyan A. Preoperative transcranial and carotid Doppler study in coronary artery bypass graft patients. *Neurosciences (Riyadh).* 2007;**12**(1):42–5. [PubMed: 21857617].
25. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975;**12**(3):189–98. [PubMed: 1202204].
26. Sayedan M, Fallh M, Noroozian M, Nejat S, Delavar A, Ghasemzadeh H. Preparation and validity of Persian version of the Mini-Mental State Examination. *J Med Council of Islamic Republic of Iran.* 2009;**25**(4):408–14.