

Original Research Article

COMPARING ALTERATION OF MMSE (MINI-MENTAL STATE EXAMINATION) SCORES AS COGNITIVE FUNCTION TEST IN GERIATRICS AFTER GENERAL AND REGIONAL ANESTHESIAFerrie Budianto^{1a}, Philia Setiawan¹, Hamzah¹, Erikavetri Yulianti²¹ Department of Anesthesiology and Reanimation, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia² Department of Psychiatry, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia^a Corresponding author: ferriebudianto2@gmail.com**ABSTRACT**

Introduction: An alteration of cognitive function in geriatrics often occurred after a surgery procedure. To do a surgery, patients would go through the process with anesthesia, whether it is general or regional anesthesia. We aimed to identify the effect of general and regional anesthesia in increasing the risk of alteration in cognitive function from geriatrics who underwent elective surgery followed by other risks. **Methods:** This observational analytic study has a total sample of 60 patients who aged 60 years or more, and half of the total sample underwent an elective surgery with general anesthesia, whereas the other half with regional anesthesia at Integrated Central Surgical Building of Dr. Soetomo General Academic Hospital in a range of October – November 2016. The cognitive function of patients was assessed with MMSE which is done in approximately 10 – 15 minutes. **Results:** There was a statistically significant correlation between age and both preoperative MMSE score also the alteration of MMSE score after 3 days in patients with regional anesthesia (P-value = 0.032; 0.044). Also, the correlation between educational status and preoperative MMSE score (P-value = 0.001). There was also a statistically significant difference in alteration of the MMSE score after 3 days between patients with general and regional anesthesia which went through the hypotension phase (P-value = 0.022; 0.003). We identified that both general and regional anesthesia could lead to alteration of MMSE score (P-value = 0.001; 0.02) and there was a statistically significant difference between both of them (P-value = 0.001). **Conclusion:** Both general and regional anesthesia could lower the cognitive function of geriatrics, especially general anesthesia which happened to have a higher risk to occur. Other factors such as age, educational status, and hemodynamic condition during surgery, had their impacts toward lowering cognitive function in geriatrics.

Keywords: Postoperative Cognitive Function; General Anesthesia; Regional Anesthesia; MMSE Score**ABSTRAK**

Pendahuluan: Perubahan fungsi kognitif pada pasien geriatri sering terjadi setelah menjalani prosedur operasi. Untuk melakukan prosedur operasi, pasien akan melalui proses anestesi, baik anestesi umum maupun anestesi regional. Peneliti ingin mengetahui efek dari anestesi umum dan regional dalam meningkatkan risiko perubahan fungsi kognitif dari pasien geriatrik yang menjalani operasi elektif diikuti dengan factor lainnya. **Metode:** Penelitian ini berdesain observasional analitik dengan jumlah sampel sebesar 60 pasien yang berusia 60 tahun atau lebih, dan setengah dari sampel tersebut menjalani operasi elektif dengan anestesi umum, sedangkan setengah lainnya dengan anestesi regional di Gedung Bedah Pusat Terpadu RSUD Dr. Soetomo dalam rentang waktu Oktober – November 2016. Fungsi kognitif pasien dinilai menggunakan MMSE Skor yang dilakukan sekitar 15-10 menit. **Hasil:** Terdapat hubungan yang bermakna antara usia pasien dengan skor preoperatif MMSE dan perubahan skor MMSE setelah 3 hari pada pasien dengan anestesis regional (nilai P = 0.032; 0.044). Juga terdapat hubungan yang bermakna antara status pendidikan pasien dengan skor awal MMSE (nilai P = 0.001). Ditemukan perbedaan yang bermakna antara skor MMSE setelah 3 hari pada pasien dengan anestesi umum dan regional yang mengalami fase hipotensi selama operasi berjalan (nilai P = 0.022; 0.003). Peneliti menemukan bahwa anestesi umum dan regional mampu menyebabkan perubahan terhadap skor MMSE (nilai P = 0.001; 0.02) dan terdapat perbedaan yang bermakna di antara keduanya (nilai P = 0.001). **Kesimpulan:** Kedua jenis anestesi, anestesi umum dan anestesi regional, mampu menurunkan fungsi kognitif pada pasien geriatri, terutama anestesi umum yang memiliki risiko lebih tinggi untuk terjadi. Faktor lain seperti usia pasien, status pendidikan pasien, dan kondisi hemodinamika selama operasi berlangsung, memiliki dampak masing-masing terhadap penurunan fungsi kognitif pada pasien geriatri.

Kata kunci: Fungsi Kognitif Pasca Operasi; Anestesi Umum; Anestesi Regional; Skor MMSE**Article info:** Received: June, 15th 2020; Revised: July, 15th 2020; Accepted: July, 27th 2020; Published: July, 29th 202

INTRODUCTION

In 2015, Indonesia reached 72 years for its life expectancy, increasing from 68.6 years in 2004. This achievement followed by an increase in geriatrics, which is 8.03% of Indonesia's total population. (1)

Attention is needed to be given more in health care towards geriatrics, such as surgery. To do surgery, we need to pay more attention to giving its anesthesia because the morbidity and mortality risks in geriatrics are higher than young adults or adults. The comprehensive and multidiscipline of evaluation in preoperative and postoperative will produce a greater outcome in geriatrics.

Postoperative complications may come in vary; central nervous system dysfunction, postoperative delirium, and postoperative cognitive dysfunction (POCD) are the most common complications in geriatrics. Delirium and POCD are usually acute and reversible if it's taken care of seriously. However, inadequate diagnosis and treatment will lead its condition to dementia.

Dementia is a neurodegenerative disorder caused by the damage of the neurons in important areas of the brain, including the hippocampus, parietal lobe, and temporal lobe. Some studies concluded that postoperative dementia happened because of an inflammatory process as a reaction towards the surgery or anesthesia itself. It's been proved by increasing pro-inflammatory mediators and cytokines in cerebrospinal fluid. Likewise, another study showed an inflammation happened in the hippocampus of a postoperative patient, which is associated with memory. (2)(3)

Potential neurotoxicity of general anesthesia to cause dementia is still a controversy. Inhalation anesthesia is suspected to increase A β protein plaque formation and neuro fibrillation which are

included in the pathogenesis of dementia. (4)(5) Several studies used mice to prove that Isoflurane inhalation increased the risk of getting POCD and dementia after surgery. (6)(7)

Researchers hypothesized that regional anesthesia should be an alternative to reduce the incidence of POCD in geriatrics. A study conducted by Mandal et al. (8) showed that an assessment of cognitive function in hip and knee surgery among geriatrics using MMSE has better results in patients with regional anesthesia rather than general anesthesia. Rasmussen et al. (9) agreed with their study also concluded that the incidence of POCD was bigger in patients with regional anesthesia after 7 days of surgery. However, Russo et al. (10) had a different result with no significant difference in cognitive function between regional and general anesthesia of postoperative patients who underwent total knee replacement surgery. Nineteen randomized trials have been reviewed by Wu et al. (11) and only one study which showed a significant difference in cognitive function between regional and general anesthesia of postoperative patients.

Mini-Mental State Examination (MMSE) is a cognitive function test that is widely used because of its simplicity in evaluating clinical conditions of patients with dementia and cognitive dysfunction. (12) Using this test, we aimed to identify the effect of general and regional anesthesia in increasing the risk of alteration in the MMSE score from geriatrics who underwent elective surgery.

METHODS

This observational analytic study has a total sample of 60 patients who aged 60 years or more, underwent an elective surgery apart from open-heart surgery or neurosurgery, and being done at Gedung Bedah Pusat Terpadu

Dr. Soetomo General Hospital in a range of October – November 2016. Half of the total sample underwent surgery with general anesthesia, whereas the other half with regional anesthesia.

There have been exclusion criteria of the sample in this study, such as: had a central nervous system dysfunction, had a mental disorder, had an addiction towards hypnotic-sedative medication, opioid, or alcohol, also a complication happened during or after surgery.

General and regional anesthesia were the independent variables of this study. Followed by the dependent variables which were MMSE score before surgery, 3 days after surgery, and 7 days after surgery. However, several patients tended to go home 5 – 6 days after surgery. The cognitive function of patients was assessed with MMSE which is done in approximately 10 – 15 minutes.

The data of this study were analyzed with SPSS Statistics 17.0. Paired t-test, Wilcoxon test, and Mann-Whitney test were used in this study.

RESULTS AND DISCUSSION

The total sample was 60 elderly patients and above 60 years old. Out of 30 patients who underwent elective surgery with general anesthesia, 11 were male patients. Whilst out of 30 other patients with regional anesthesia, male patients were dominating with 17 in total. Based on the result of the Chi-Square test, there was no statistically significant difference between gender and all MMSE scores (P-value = 0.911; 0.871; 0.654), this result showed that males and females have similar probability to encounter dementia.

In patients with general anesthesia, 26 patients had an age range of 60 – 69 years old, whereas 2 patients each in the age range of 70 – 79 years old and 80 years old. Twenty patients also dominated in the age range of 60

– 69 years old, followed by 9 patients in the age range of 70 – 79 years old, and 1 patient aged 80 years.

Table 1. The Correlation between Age Range and Preoperative MMSE Score

Age Range	Preoperative MMSE Score (n=60)			P-Value
	11 – 20	21 – 26	27 – 30	
60 – 69	1 (1.67%)	30 (50%)	15 (25%)	0.032*
70 – 79	0 (0%)	9 (15%)	2 (3.33%)	
≥80	1 (1.67%)	2 (3.33%)	0 (0%)	

*Chi-Square test

Table 2. The Correlation between Age Range and Alteration of MMSE Score After 3 days in patients with General and Regional Anesthesia

Age Range	General Anesthesia (n=30)			P-Value	Regional Anesthesia (n=30)		P-Value
	0	1-2	3-4		0	1-2	
60 – 69	4 (13.3%)	17 (56.6%)	5 (16.7%)	0.138*	18 (60%)	2 (6.7%)	0.044*
70 – 79	0 (0%)	0 (0%)	2 (6.7%)		6 (20%)	3 (10%)	
≥80	0 (0%)	1 (3.3%)	1 (3.3%)		0 (0%)	1 (3.3%)	

*Chi-Square test

Based on table 1, there was a statistically significant correlation between age and preoperative MMSE score after being tested with the Chi-square test (P-Value = 0.032). Table 2 showed that there was no correlation between age and the alteration of the MMSE score after 3 days in patients with general anesthesia (P-value = 0.138). But, we got a different value for the regional anesthesia group. There was a significant correlation between age and the alteration of the MMSE score after 3 days in patients with regional anesthesia (P-Value = 0.044). This result was similar to a study conducted by Crosby et al. (13) which showed a decline of brain mass from 95% in young adults to 80% in geriatrics.

Neurons happened to shrink in size, a number of synapses, and dendritic complexity. Aging was hypothesized to decrease the functional brain which led into dementia. (13)(14)

Eleven patients in general anesthesia group were dominating with educational status as Junior High School alumni, whereas the same number of patients were equally dominating with educational status as Junior High School alumni and Elementary School alumni with a total of 12 patients each in regional anesthesia group.

Table 3. The Correlation between Educational Status and Preoperative MMSE Score

Educational Status	Preoperative MMSE Score (n=60)			P-Value
	11 – 20	21 – 26	27 – 30	
Undergraduate	0 (0%)	0 (0%)	3 (5%)	
Senior High School	0 (0%)	1 (1.67%)	8 (13.3%)	
Junior High School	0 (0%)	18 (30%)	5 (8.33%)	0.001*
Elementary School	1 (1.67%)	19 (31.7%)	1 (1.67%)	
Didn't Graduate Elementary School	1 (1.67%)	2 (3.33%)	0 (0%)	

*Chi-Square test

Based on Table 3 there was a statistically significant correlation between educational status and preoperative MMSE score after being tested with the Chi-Square test (P-value = 0.001). Emily Sharp et al. conducted a study which showed that a higher educational status reflected a higher capacity and better cognition of the brain, it would decrease the risk of dementia to happen. Cognitive reserve theory hypothesized that a person with low educational status was more susceptible to experience brain damages compared to the ones who had a higher educational status. (15) The different result was getting from the correlation between Educational status and the alteration of MMSE Score both in general dan

regional anesthesia. There was no statistically significant correlation with P-Value = 0.223 (general anesthesia) and P-Value = 0.572 (regional anesthesia).

Most of the patients both in general and regional anesthesia group suffered from hypotension phase during surgery, with 22 patients in general anesthesia group and 25 patients in the other.

Table 4. The Correlation between Hypotension and Alteration of MMSE Score After 3 Days in Patients with General Anesthesia

Hypotension	MMSE Score after 3 days (General anesthesia) (N=30)			P-Value
	0	1 – 2	3 – 4	
Yes	0 (0%)	3 (10%)	5 (16.7%)	0.022*
No	4 (13.3%)	15 (50%)	3 (10%)	

*Chi-Square test

Table 5. The Correlation between Hypotension and alteration of MMSE score after 3 days in patients with regional anesthesia

Hypotension	MMSE Score after 3 days (Regional anesthesia) (N=30)		P-Value
	0	1 – 2	
Yes	1 (3.33%)	4 (13.3%)	0.003*
No	23 (76.7%)	2 (6.67%)	

*Chi-Square test

Based on Tables 4 and 5, there was a statistically significant correlation in the alteration of the MMSE score after 3 days between patients with general and regional anesthesia which went through the hypotension phase after being tested with Chi-Square test (P-value = 0.022; 0.003). This result was similar to a study conducted by Doods et al. (16), which after 5 days of retropubic prostatectomy surgery, the patients who went through the hypotension phase during surgery had a lowering cognitive function then recovered in the sixth week.

The duration of anesthesia given to each group of patients was mostly done below or equal to 180 minutes. Only 8 patients were given general anesthesia above 180 minutes, whereas regional anesthesia was given to only 6 patients. There was no statistically significant correlation between the duration and alteration of the MMSE score in both groups after being tested with the Chi-Square test (P-value = 0.378). Gelmanas et al. (17) had a similar result concerning the same variable.

Table 6. The Comparison between the preoperative and after 3 days MMSE Score in General and Regional Anesthesia

MMSE Score	General Anesthesia (n=30)		Regional Anesthesia (n=30)	
	Mean±SD	P-Value	Mean±SD	P-Value
Preoperative	25.13±2.801	0.001*	24.8±2.52	0.02**
After 3 days	23.43±3.431		24.6±2.68	

*paired T-Test **Wilcoxon Test

Table 7. The Comparison between the MMSE Score of General and Regional Anesthesia

The Kind of Anesthesia	MMSE Score	
	Mean±SD	P-Value
General Anesthesia	1.7 ± 1.088	0.001*
Regional Anesthesia	0.23 ± 0.504	

*Mann-Whitney test

Based on the result of Paired T-Test, there was significant difference between preoperative and after 3 days MMSE Score in General anesthesia patient (P-Value = 0.001). The Regional anesthesia group tested with the Wilcoxon test and there was significant difference between preoperative and after 3 days MMSE Score (P-Value = 0.02) (Table 6). We also identified that there was a statistically significant difference between the alteration of the MMSE score with general and regional

anesthesia after being tested with the Mann-Whitney test (P-value = 0.001). In other words, a lowering cognitive function would happen more often in patients with general anesthesia compared to the patients with regional anesthesia.

With several remaining data of patients who were still available until 7 days after the surgery, 33% of patients in the general anesthesia group happened to lose 2 points of their MMSE score and the rest only lost 1 or 0 points. Even in regional anesthesia group, no patient was found with an alteration of the MMSE score. This result might lead to the hypothesis of reversible lowering cognitive function.

CONCLUSION

Both general and regional anesthesia could lower the cognitive function of geriatrics, especially general anesthesia which happened to have a higher risk to occur. Other factors such as age, educational status, and hemodynamic condition during surgery, had their impacts toward lowering cognitive function in geriatrics.

Conflict of Interest

There is no conflict of interest in this research nor on the writing of the article.

REFERENCES

1. Kementerian Kesehatan Republik Indonesia.
<http://www.depkes.go.id/article/print/16031000003/menkes-lansia-yang-sehatlansia-yang-jauh-dari-demensia.html>.
2. Gao L, Taha R, Gauvin D, Othmen, Wang Y, Blaise G, Postoperative cognitive dysfunction after cardiac surgery, *Chest* 2005, 128: 3664-70.

3. Maze M, Cibelli C, Grocott HP, Editorial view: Taking the lead in research into post-operative cognitive dysfunction, *Anesthesiology* 2008,108; 1-2.
4. Xie Z, Culley DJ, Dong Y, Zhang G, Zhang B, Moir RD, et al. The common inhalation anesthetic isoflurane induces caspase activation and increases amyloid beta-protein level in vivo. *Ann Neurol* 2008; 64: 618–27.
5. Planel E, Richter KE, Nolan CE, Finley JE, Liu L, Wen Y, et al. Anesthesia leads to tau hyperphosphorylation through inhibition of phosphatase activity by hypothermia. *J Neurosci* 2007; 27: 3090–3097.
6. Culley DJ, Baxter M, Yukhananov R, Crosby G. The memory effects of general anesthesia persist for weeks in young and aged rats. *Anesth Analg* 2003; 96: 1004–1009.
7. Culley DJ, Baxter MG, Yukhananov R, Crosby G. Long-term impairment of acquisition of a spatial memory task following isoflurane–nitrous oxide anesthesia in rats. *Anesthesiology* 2004; 100: 309–314.
8. Mandal Sripurna et al. Impact of general versus epidural anesthesia on early postoperative cognitive dysfunction following hip and knee surgery. *Journal of Emergency, Trauma and Shock* 2011; 14:11.
9. Rasmussen LS et al. Does anaesthesia cause postoperative cognitive dysfunction? A randomized study of regional versus general anaesthesia in 438 elderly patients. *Acta Anaesthesiol Scand* 2003; 47: 260-266.
10. Russo P, et al. Cognitive effects after epidural vs general anaesthesia in older adults a randomized trial. *JAMA* 1995; 27(1).
11. Wu Christopher, Hsu Wesley et al. Postoperative cognitive function as an outcome of regional anaesthesia and analgesia. *Regional Anesthesia and Pain Medicine* 2004; 29: 257-268.
12. 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: 189–198.
13. Crosby G, Culley DJ, Anesthesia, The Aging Brain and the Surgical Patients, *Can J Anesth*: 2003; 50(6).
14. Maze M, Cibelli C, Grocott HP, Editorial view: Taking the lead in research into postoperative cognitive dysfunction, *Anesthesiology* 2008, 108; 1-2.
15. Sharp, Emily Schoenhofen. The Relationship between Education and Dementia An Updated Systematic Review. *Alzheimer Dis Assoc Disord*. 2011 October; 25(4): 289–304.
16. Dodds C, Allison J, Postoperative cognitive deficit in the elderly surgical patients, *Br J Anaesth* 1998, 81: 449 – 62.
17. Gelmanas A., Bukauskas T., Macas A. Postoperative cognitive dysfunction in geriatric patients after orthopedic surgery. *Acta Medica Lituanica* 2012; 19(3): 108–114.