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Correlation between hypertension and cognitive function in elderly

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Abstract. Hypertension and cognitive impairment are common disorders among elderly adults, and their prevalences tend to rise as the population ages. This study aimed to determine the correlation between hypertension and cognitive function in elderly. It was a cross-sectional study involving 62 elderly subjects. All subjects underwent physical and neurologic examination and Montreal Cognitive Assessment-Indonesian Version (MoCA-INA) to assess cognitive function. This study included 62 subjects consisted of 26 males (41.9%) and 36 females (58.1%). There were 24 subjects (38.2%) with hypertension and 38 (61.3%) normal elderly subjects. The mean age was 65.71±4.49 years old. There were no significant differences in demographic characteristics, total MoCA-INA scores, and scores based on cognitive domains between two groups, except for visuospatial and executive function (p=0.026). There was a significant correlation between hypertension and visuospatial and executive function (r=0.301, p=0.017). Hypertension is correlated with cognitive impairment mainly on visuospatial and executive function in elderly.

1. Introduction
Hypertension and cognitive impairment are common disorders among elderly adults, and their prevalences tend to rise as the population ages. The association between high blood pressure (BP) and cognitive impairment has been a topic of great interest in the past few decades.[1] Several recent studies have shown an association between hypertension in global cognitive function, attention, visuospatial skill, memory and executive function.[2-6]

Dementia is a major and growing global public health problems affecting 47.5 million people worldwide with 7.7 million new diagnosed cases per year.[3] It was 35.6 million people lived with dementia worldwide in 2010, with numbers expected almost to double every 20 years, to 65.7 million in 2030 and 115.4 million in 2050. In 2010, 58% of all people with dementia lived in countries with low or middle incomes, with this proportion anticipated to rise to 63% in 2030 and 71% in 2050.[7] Alzheimer disease (AD) and cerebrovascular diseases are the second leading causes of cognitive impairment, accounting for almost 80% of cases and often having a mixture of both pathologies.[6] Vascular dementia contributes to nearly 25-30% of all dementia cases. With an increase in life expectancy and the growing prevalence of uncontrolled hypertension, the worldwide incidence of patients with dementia is expected to rise even further.[3]

The functional and anatomic changes produced by high BP on the brain’s vasculature system constitute a modifiable risk for vascular dementia and may play a significant role in Alzheimer’s disease (AD).[4] Among vascular risk factors, chronic arterial hypertension is a major contributor to
cognitive impairment. Hypertension, a highly prevalent disease affecting an estimated 1 billion individuals worldwide, is the leading cause of global disease burden and overall health loss. The brain is one of the main target organs affected by hypertension. Thus, excluding age, hypertension is the most important risk factor for cerebrovascular pathology leading to stroke and dementia. Hypertension has been associated with reduced abstract reasoning (executive dysfunction), slowing of mental processing speed, and, less frequently, memory deficits.[6] Cerebral blood vessels are the main target of the deleterious effects of hypertension on the brain. The resulting structural and functional cerebrovascular alterations underlie many of the neuropathological abnormalities responsible for the cognitive deficits, including white matter damage, microinfarcts, microbleeds, silent brain infarcts, and brain atrophy.[6] Therefore it is important to assess cognitive function in hypertensive patients.

The Montreal Cognitive Assessment (MoCA) has been widely used in the cognitive assessment. The MoCA assess several cognitive domains including executive function, visuospatial function, attention and concentration, memory, language, calculation, and orientation. The Indonesian version of MoCA, namely MoCA-INA has been developed and validated in Indonesia, and so it can be used as a cognitive tool. This study aimed to determine the correlation between hypertension and cognitive function in elderly across several domains.

2. Methods
It was a cross-sectional study involving 62 subjects which were from the Memory Clinic Neurology Department Adam Malik General Hospital Medan North Sumatera Indonesia, between November 2016 and July 2017. Inclusion criteria were: age equal or more than 60 years-old, compos mentis and fully cooperative, speak Bahasa Indonesia fluently, able to read and write, and gave written consent to be included in the study. Subjects who were medically unstable (delirium) or have other psychiatric disorders, had an aphasia, history of stroke, dementia and diabetes mellitus were excluded from the study. All subjects underwent physical and neurologic examination and Montreal Cognitive Assessment-Indonesian Version (MoCA-INA).

All statistical procedures were with SPSS. The correlation between MoCA-INA scores and hypertension was measured using the Spearman correlation, and the comparison of MoCA-INA score between groups was measured using t-independent test. The study was with approval obtained from the Health Research Ethical Committee Medical Faculty of Universitas Sumatera Utara/H. Adam Malik General Hospital.

3. Results
This study included 62 subjects consisted of 26 males (41.9%) and 36 females (58.1%). There were 24 subjects (38.2%) with hypertension and 38 (61.3%) normal elderly subjects. The mean age was 65.71 years old with SD 4.49. Most of the subjects aged between 60 and 64 years old (28 subjects (45.2%)) and the fewest subjects aged 75-79 years old (4 subjects (6.5%)). The mean MoCA-INA score was 23.08 ± 3.60. There were no significant differences in demographic characteristics between groups. Table 1 summarizes the subjects’ characteristics and cognitive scores between two groups.

The global cognitive performance did not differ significantly between two groups, as well as on several cognitive domains that assessed with MoCA-INA, but there was a significant difference in visuospatial and executive function, which were assessed using a subset of trail making test A (TMT A), copying cube and clock drawing. Table 2 shows the differences of MoCA-INA scores between two groups based on cognitive domains.

The MoCA-INA score showed a positive correlation with hypertension, but this was not statistically significant, as well as naming, abstraction and delayed recall. The visuospatial and executive function showed a significant and good positive correlation with hypertension. Table 3 shows the correlation between hypertension and MoCA-INA scores based on cognitive domains.

Table 1. It is characteristics of the hypertensive and normotensive groups.
Characteristic                  Total (n=62)                  Hypertensive (n=24)                  Normotensive (n=38)                  p value
Age (years), mean ± SD         65.71 ± 4.49                  65.63 ± 4.2                  65.76 ± 4.73                  NS (0.9)
Age groups, years old
60-64                          28 (45.2)                  11 (45.83)                  17 (44.73)                  NS (0.9)
65-69                          23 (37.1)                  9 (37.50)                  14 (36.84)                  NS (0.9)
70-74                          7 (11.3)                   3 (12.50)                  4 (10.52)
75-79                          4 (6.5)                    1 (4.16)                    3 (7.89)
Sex (n [%])
Male                          26 (41.9)                  10 (41.6)                  16 (42.1)                  NS (0.204)
Female                        36 (58.1)                  14 (58.4)                  22 (57.8)
Educational Level
Primary                       8 (12.9)                   3 (12.50)                  5 (13.15)
Junior High School            11 (17.7)                  6 (25.00)                  5 (13.15)                  NS (0.98)
High School                   27 (43.5)                  7 (29.16)                  20 (52.63)
College/University            16 (25.8)                  8 (33.33)                  8 (21.05)
Occupation
Unemployed                    19 (30.6)                  6 (25.00)                  13 (34.21)
Housewife                     23 (37.1)                  8 (33.33)                  15 (39.47)
Employee                      7 (11.3)                   3 (12.50)                  4 (10.52)                  NS (0.82)
Entrepreneur                  11 (17.7)                  5 (20.83)                  6 (15.78)
Farmer                        2 (3.2)                    2 (8.33)                    0 (0)
MoCA-INA score               23.08 ± 3.60                22.63 ± 4.31                23.37 ± 3.09                NS (0.468)

Table 2. It is a comparison of MoCA-INA scores between two groups.

| Cognitive Domain                      | Hypertensive (n=24) Mean ± SD | Normotensive (n=38) Mean ± SD | p value |
|---------------------------------------|-------------------------------|-------------------------------|---------|
| Visuospatial and Executive Function   | 2.38 ± 4.31                  | 2.82 ± 0.86                   | 0.026*  |
| Naming                                | 2.67 ± 0.63                  | 2.87 ± 0.41                   | 0.177   |
| Attention                             | 4.63 ± 0.16                  | 4.71 ± 1.03                   | 0.823   |
| Language                              | 2.46 ± 0.77                  | 2.32 ± 0.66                   | 0.462   |
| Abstraction                           | 1.38 ± 0.57                  | 1.47 ± 0.50                   | 0.495   |
| Delayed Recall                        | 3.54 ± 1.20                  | 3.71 ± 0.86                   | 0.566   |
| Orientation                           | 5.54 ± 0.97                  | 5.21 ± 0.99                   | 0.202   |

Table 3. Correlation between hypertension and MoCA-INA scores based on cognitive domains.

| Cognitive Scores                      | Hypertension |
|---------------------------------------|--------------|
|                                       | r  | p     |
| MoCA-INA                              | 0.06| 0.646|
| Visuospatial and Executive Function   | 0.301| 0.017*|
| Naming                                | 0.194| 0.131|
| Attention                             | -0.051| 0.694|
| Language                              | -0.137| 0.289|
| Abstraction                           | 0.077| 0.554|
| Delayed Recall                        | 0.048| 0.712|
| Orientation                           | -0.191| 0.137|

4. Discussion
Our data show a correlation between hypertension and cognitive function. The relation of hypertension and cognitive function is frequently studied by comparing the cognitive performance of people with normal BP (normotensive) with that of hypertensive patients. Commonly assessed cognitive functions include attention, learning and memory, executive functions (i.e. self-regulatory
behaviors like planning and organization, mental flexibility, and response inhibition), visuospatial skills, psychomotor abilities, perceptual skill and language abilities.[5]

The result of this study indicates that hypertension is associated with cognitive impairment, especially with visuospatial and executive function in elderly. This finding is consistent with the previous study that found the association between elevated blood pressure and a selective impairment in executive function in healthy community-dwelling elders and found that elevated BP is an independent correlate of frontal executive dysfunction.[2]

A study by Vicario et al. (2005) involving sixty elderly hypertensive patients compared with 30 normotensive individuals also found that the hypertensive patients evinced impairment in all test compared to the normotensive patients. Deficits in attention speed and executive function were present in 46% of hypertensive patients compared to 13% of normotensive subjects (p<0.005). Compared with the control group, the hypertensive patients revealed more deficits in skills involving delayed recall and prefrontal region skills.[4]

Our study shows no significant difference in global cognitive function between hypertensive patients and normal control, as indicated by MoCA-INA score 22.63±4.31 and 23.37±3.09, respectively. This data is different from finding in a study by Muela et al. (2017), in which they found a significant difference of MoCA score between normotensive (25.48±3.21), hypertension stage 1 (24.93±2.83) and hypertension stage 2 (23.36±3.60). They also found that cognitive impairment was more frequent in patients with hypertension, and this was related to hypertension severity. Our study did not classify hypertension further and could attribute to this different finding.[5]

The mechanisms linking blood pressure to cognitive impairment are complex and not fully understood.[3] Microvascular dysfunction and damage induced by hypertension lead to white matter disease, microinfarcts, and microhemorrhages, alterations which closely correlated with the cognitive dysfunction. Hypertension has major effects on the regulation of the cerebral circulation, which may impair brain structure and function by reducing vascular reserves and promoting ischemic injury.[8] The abnormalities associated with aging impact brain circulation causing a reduction in resting cerebral blood flow with dysfunction of cerebral regulatory mechanisms which are further potentiated by arterial hypertension.[9,10] The number of cerebral capillaries in the cortex is reduced, and their basement membranes become thickened and fibrotic.[10] These alterations result in a reduction of resting cerebral blood flow (CBF), attenuation of cerebrovascular reserves and dysfunction of the mechanisms regulating the cerebral circulation. Hypertension might potentiate these age-related alterations. The hypertension-related cognitive decline is a consequence of the interplay between functional blood flow reorganization and brain vascular damage.[3,8-10]

Subsequently, hypertension-related cognitive dysfunction develops as a result of the imbalance inautoregulation of cerebral blood flow and cerebral vascular alterations. Also, arterial stiffness may explain the association between hypertension and cognitive dysfunction.[11] The negative impact of hypertension on total brain perfusion remained reduced irrespective of patients’ age. Reduced total brain perfusion predicted a decrease in cortical thickness whereas antihypertensive therapy was unrelated to total cerebral perfusion or cortical thickness.[12]

Hypertension gives rise to vascular modifications which affect blood flow and cerebral metabolism. Cognitive disorders maybe associated with the presence of focal ischaemic lesions (infarction, lacune) and/or chronic ischemia of the white matter due to small cerebral artery disease (arteriosclerosis, lipohyalinosis).[13] White matter hyperintensities were associated with an increased risk of dementia in the general population. Changes in white matter commonly occur in the elderly. However, the mechanisms underlying their decrease are not fully understood. Cerebral small vessel disease importantly contributes to a reduction in white matter which has been shown to be associated with an increased risk of stroke, cognitive dysfunction, dementia.[13,14]

The most interesting observation in our study was the impairment of executive function—cognitive function in the brain’s prefrontal areas. It is the most developed region and is responsible for processing the most complex intellectual tasks, concentrating perceptive, volitional, cognitive and emotional aspects.[4] Our study used a subset of TMT-A, clock drawing test and verbal fluency in
MoCA—INA to assess executive function. Executive function involves multiple brain processes and consequently is the cognitive domain that is most difficult to assess and has the most heterogeneity in measurements across studies. Executive function is of particular importance for daily life because of the role it plays in decision making and problem-solving, critical tasks for self-management of chronic illnesses. The most common tests used were the Controlled Oral Word Association Test (word fluency), category fluency (e.g., animal naming), and the Trail Making Test Part B. The word fluency test requires subjects to generate as many words as possible beginning with the same letter of the alphabet (F, A, or S) in 60 seconds. On average, older adults without cognitive impairment generate 12 to 16 words per minute.[6]

Frontal-executive dysfunction may be more common than expected in elderly persons because of the prevalence of hypertension and other cardiovascular risk factors increase with age. Ischemic damage to small vessels in fronto-subcortical regions may selectively impair executive functions.[2] When the brain begins to age, the frontal—cortical regions becomes reduced by 20% in seniors between 65 and 80 years of age as a result of atrophy and a decrease in neuronal population. The defferentation of the frontal lobes as a result of lesions in specific circuits (prefrontal, dorsolateral, orbitofrontal, and anterior cingulate) that connect the subcortex with this region brings about “executive dysfunction”. It would be characterized by the impaired performance of mental operations, psychomotor retardation, attention deficit (distractibility), visual and spatial alterations, difficulty in planning and starting an activity, apathy, and loss of inhibition.[4]

Our study has several limitations. First, the design of this study was cross-sectional, so we can not establish a causal relationship between hypertension and cognitive impairment, specifically visuospatial and executive function. Second, our study sample is relatively small and our study was carried out in a select group of patients with hypertension referred to a hospital, limiting the generalizability of our findings to other populations.

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