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Research Article

Masked Hypertension is Associated With Cognitive Decline in Geriatric Age–Geriatric MASked Hypertension and Cognition (G-MASH-cog) Study

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Abstract

Background: Masked hypertension is described as high ambulatory blood pressure measurements (ABPM) where office blood pressure measurements are normal. Effect of hypertension on cognitive functions is well known. However, the effect of masked hypertension on cognitive functions is unclear. The aim of this study is to examine the relationship between masked hypertension and cognitive functions.

Methods: One hundred-two normotensive patients admitted to the Geriatric Medicine outpatient clinic were included. Exclusion criteria were hypertension, dementia, major depression, and usage of antihypertensive medication. All patients underwent ABPM procedures and average daytime blood pressure, mean blood pressure at night and the 24-hour average blood pressure measurements were recorded. Comprehensive geriatric assessment tests and neuropsychological tests were administered. The diagnosis of masked hypertension was based on the definitions in the 2013 guideline of the European Society of Cardiology.

Results: Forty-four patients (43%) were diagnosed with masked hypertension. Patients with masked hypertension had significantly lower scores on Mini-Mental State Examination (MMSE) test, Quick Mild Cognitive Impairment Test (QMCI), and Categorical Fluency Test than the normotensive patients ($p = .011$; $p = .046$; and $p = .004$; respectively). Montreal Cognitive Assessment Scale test score was lower in masked hypertension, although this was not statistically significant.

Conclusion: This study may indicate that geriatric patients with masked hypertension, compared to normotensive patients have decreased cognitive functions. Masked hypertension should be kept in mind while assessing older adults. When masked hypertension is detected, cognitive assessment is essential to diagnose possible cognitive dysfunction at early stage.

Keywords: Masked hypertension—Cognitive functions—Geriatrics

Ambulatory blood pressure measurement (ABPM) has become increasingly common in clinical daily practice in recent years. Ambulatory blood pressure measurement is an extremely valuable method for determining white coat hypertension and masked hypertension. Recent studies show that 10–40% of the patients, who were known as "normotensive" previously, were diagnosed as "hypertensive" after ABPM (1–4). This condition is called masked hypertension or isolated ambulatory hypertension. This phenomenon can be diagnosed with ABPM or home measurements (5).

The relationship between blood pressure and cognitive functions has two aspects. Follow-up studies showed that hypertension in middle ages, causes a decline in cognitive functions in older age

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and increases the risk of dementia by causing vascular damage. On the other hand, hypotension in older age reduces cerebral perfusion and therefore, it is associated with cognitive dysfunction. In one study, it was shown that Alzheimer's Diseases is negatively correlated with hypertension in geriatric age (6). There are great number of studies evaluating the relationship between hypertension and cognitive function. Results of UK MRC and HOPE studies, in which hypertensive patients were monitored with antihypertensive treatment, showed no effect of hypertension treatment on dementia (6,7). However, later studies showed decreased risk of dementia in older age by controlling hypertension in middle age. Results of PROGRESS study, Hypertension in the Very Elderly Trial-cognitive, the Study on Cognition and Prognosis in the Elderly, and Syst-Eur studies showed that controlling blood pressure pharmacologically prevents dementia (8–11). In a study conducted after the publication of JNC-8, patients with blood pressure >150 mmHg had lower MMSE test scores and a higher risk of developing mild cognitive impairment (12). On the other hand, low blood pressure is known to have a negative effect on cognitive functions in geriatric age. Kungsholmen Project shows that systolic blood pressure under <140 mmHg is associated with Alzheimer's Disease (AD) (13). In a study that took place in Turkey, 193 Alzheimer's Disease patients and 1860 controls were compared, and hypertension prevalence was found lower in the AD than the control group (6). Influence of masked hypertension on cognitive functions is not known. Depending on the studies indicating that hypertension is a risk factor for cognitive dysfunction, and the results of Honolulu Asia Aging Study demonstrating a link between lower brain volume, neuritic plaques, and hypertension, we hypothesized that masked hypertension, which is usually an overlooked diagnosis, may be associated with cognitive functions (14).

Different rates of masked hypertension are encountered in prevalence studies. It is reported as 5% in Spanish children (6–18 years of age), 10.2% in Turkish middle aged adults (mean age 57.1 ± 9.1), and 40% in geriatric population (mean age 70 ± 6.5) (2,3,15,16). Masked hypertension is associated with arterial and ventricular damage in the general population (17). Follow-up studies revealed that patients with masked hypertension have similar cardiovascular and renal morbidity as hypertensive patients (18–20). Furthermore, increased cardiovascular and non cardiovascular mortality was determined in patients with increased blood pressure determined by ABPM (21). Despite the evidence regarding the end organ effects of masked hypertension, its effect on cognitive function has not been studied.

Although the relationship between hypertension and cognitive function is well studied, to the best of our knowledge, there is no data regarding the effect of masked hypertension on cognitive function in older adults. The aim of this study was to fill this gap and evaluate the cognitive functions in patients diagnosed with masked hypertension and to compare with normotensives.

Patients and Method

Patients

The study was conducted in a geriatric medicine outpatient clinic of a university hospital between December 2015 and May 2016. Consecutive 2106 patients, who were all Caucasians, admitted during the study period were examined. Consecutive 102 patients (60 female/42 male) aged 65 years and over without a history of hypertension with an office blood pressure measurement lower than 140/90 mmHg, who did not meet the exclusion criteria, and agreed to participate in the study were included after receiving written and verbal informed consent.

Exclusion criteria were as follows:

- known hypertension or usage of any anti-hypertensive medication
- diagnosis of dementia
- diagnosis of major depression

Number of patients excluded because of hypertension was 1378, dementia was 316, depression was 235, and usage of antihypertensive drug was 44. Twenty-six of the eligible patients did not agree to participate in the study because they did not want to come to another visit for the study. Five eligible patients could not be enrolled because they were morbid obese and the cuff diameter of the ABPM device was not suitable.

All patients underwent comprehensive geriatric assessment. Cognitive assessments were performed within the scope of it. This study was approved by the local ethics committee.

Comprehensive Geriatric Assessment and Cognitive Assessment

Demographic characteristics, comorbidities, and use of medications were recorded. Comprehensive geriatric assessment was performed to each patient. Geriatric syndromes including depression, falls, incontinence, malnutrition, polypharmacy, and osteoporosis were assessed within this assessment. Geriatric syndromes were diagnosed after this assessment. For objective evaluation, KATZ Activities of Daily Living (KATZ) scale, Lawton Brody Instrumental Activities of Daily Living scale (Lawton-Brody), short form of Mini-Nutritional Assessment (MNA-sf), and Yesevage Geriatric Depression Scale short form were performed to all patients (22–25). Additionally, Mini Mental State Examination (MMSE), Clock Drawing Test, Montreal Cognitive Assessment Scale (MOCA), Trail Making Test, Forward and Backward Digit Span Test, Categorical Fluency Test, and Quick Mild Cognitive Impairment Screening Test (QMCI-TR) were performed to all patients for cognitive assessment (26–29).

Mini Mental State Examination (MMSE) is a test to assess cognitive ability by examining orientation, attention and calculation, recall, registration, language, and ability to follow simple commands. It has 11 items with a total score 0–30 and a low score being indicative of cognitive impairment. Montreal Cognitive Assessment Scale (MOCA) is a cognitive screening test that measures executive functions, memory, attention, working memory, visual-spatial skills, concentration, orientation, and language. The score can range from 0 to 30. The sum of all items results in an overall score, in which higher score indicating better cognitive performance. Quick Mild Cognitive Impairment Screening Test (QMCI-TR) is a useful tool in differentiating mild cognitive impairment from normal cognition. It consists of six different categories which are orientation, registration, clock drawing, delayed recall, verbal fluency, and logical memory. It is scored out of 100 points. In Trail Making Test (TMT)-A, the participants' aim is to draw a line between the numbers in correct order. When an incorrect response is made, the participant is warned to indicate that an alternative response should be made. The outcome measure was the time taken to complete the test. Digit Span Test requires the examiner to verbally present digits at a rate of one per second. The forward test requires the patient to repeat the digits verbatim. The backward test requires the patient to repeat the digits in reverse order. The number of the digits increases by one until the patient consecutively fails two trials of the same digit length.

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In Categorical Fluency Test, patients are asked to count animals as many as they can within one minute. Clock Drawing Test assesses visual-spatial activities in which patients are asked to draw a clock, write down all the numbers and point the time as ten past eleven (26–29).

Ambulatory Blood Pressure Measurement

Ambulatory blood pressure measurement device (CONTEC ABPM 50 ®) which automatically measures and records blood pressure was installed to the passive arm of the patients in the morning. It was programmed to perform a measurement every 15 minutes between 07:00 AM and 22:00 PM and every 60 minutes after 22:00 PM. Patients wore the ABPM for 24 hours.

Ambulatory blood pressure measurements is a method for establishing the average of daily, daytime, and overnight blood pressure with a tool and perform measurements with a computer, every 15–20 minutes in daytime and every 30–60 minutes overnight (30).

Normal values for blood pressure measured by ABPM are:

- ≤130/80 mmHg for 24 hours average blood pressure
- ≤135/85 mmHg for daytime average blood pressure
- ≤120/70 mmHg for overnight average blood pressure (30–34).

Masked hypertension is diagnosed when the patients whose blood pressure values are under 140/90 mmHg in office measurements, but the average of ambulatory blood pressure is higher than any of the normal values described above. Patients with blood pressure levels in normal range in all three different groups of measurements were considered as the normotensive group. Blood pressure values recorded by the device were interpreted with the aid of the computer software of the device and measurements were recorded. Patients were also recommended to measure their own blood pressure at home by themselves, four times a day (with 1–2 minutes intervals, 2 times in the morning and 2 times in the evening, after 10 minutes of rest and without using caffeine products or smoking priorly). The arithmetic average of home blood pressure measurements was recorded.

Statistical Analyses

Statistical analysis was performed by using SPSS software version 15.0. The variables were evaluated by visual (histograms, probability plots) and analytical methods (Kolmogorov–Smirnov/Shapiro–Wilk test) to determine whether or not they are normally distributed. Descriptive analyses are presented using means and standard deviation (mean ± SD) for normally distributed variables, and by median, minimum–maximum values for skew distributed variables. Categorical variables were expressed as numbers and percentages (%). For comparison between groups, Mann–Whitney *U* test and *t*-test were used for continuous variables, and chi-square test was used for categorical variables. p value <.05 was considered significant. Pearson or Spearmen correlation analysis were performed for examining correlations. Multivariable linear regression was used to examine the relationship between masked hypertension and cognitive function. Unadjusted analyses were performed in Model 1. In Model 2, results were adjusted for age, sex, and education. This was the primary focus of the study. In Model 3, other covariates including alcohol consumption, smoking, depression, and diabetes mellitus were added to the regression analysis. A 5% type I error level was used to infer statistical significance.

Results

Total number of 102 patients was included in the study. The demographic characteristics of participants are given in Table 1. Forty-four patients (43.1%) were diagnosed with masked hypertension by ABPM. Mean age, gender, and other general characteristics were similar between masked hypertension and normotensive groups (Table 1).

Frequencies of chronic diseases and geriatric syndromes including polypharmacy, falls, osteoporosis, depression, urinary incontinence, and malnutrition were similar between groups (Table 1).

The results of ABPM are shown in Table 2. Patients with masked hypertension had higher 24 hours average, daytime, and overnight blood pressure levels in office measurements, home measurements, and ABPM than the normotensive group (p = .001).

Table 1. Demographic Characteristics, Chronic Diseases, and Geriatric Syndromes of the Patients

	Total (n = 102)	Masked Hypertension (n = 44)	Normotensive (n = 58)	p value
Age	71.92 ± 5.72	72.89 ± 5.53	71.19 ± 5.79	.13
Gender (male)	42 (41.2%)	19 (43.2%)	23 (39.7%)	.72
(Female)	60 (58.8%)	25 (56.8%)	35 (60.3%)	
Education level				
Primary school/illiterate	57 (55.9%)	30 (68.2%)	27 (46.6%)	
Secondary school	15 (14.7%)	3 (6.8%)	12 (20.7%)	.11
High school	11 (10.8%)	4 (9.1%)	7 (12.1%)	
University	19 (18.6%)	7 (15.9%)	12 (20.7%)	
Smoker	16 (15.7%)	6 (13.6%)	10 (17.2%)	.47
Alcohol user	12 (11.8%)	5 (11.4%)	7 (12.1%)	.91
Number of used drugs	1 (0–6)	2 (0–6)	1 (0–6)	.68
History of falling	2 (2%)	0	2 (3.4%)	—
Osteoporosis	25 (24.5%)	11 (25%)	14 (24.1%)	.92
Depression	21 (20.6%)	11 (25%)	10 (17.2%)	.33
Urinary incontinence	8 (7.8%)	2 (4.5%)	6 (10.3%)	.46
Malnutrition	1 (1%)	0	1 (1.7%)	—
Diabetes mellitus	22 (21.6%)	10 (22.7%)	12 (20.7%)	.80
Coronary artery disease	5 (4.9%)	2 (4.5%)	3 (5.2%)	.88
Hyperlipidemia	22 (21.6%)	10 (22.7%)	12 (20.7%)	.80

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Table 2. Results of Ambulatory Blood Pressure Measurements

	Total (n = 102)	Masked Hypertension (n = 44)	Normotensive (n = 58)
Office measurements			
Systolic	128.3 ± 12.0	130.2 ± 10.5	126.8 ± 12.9
Diastolic	79.5 ± 8.8	80.1 ± 8.3	79 ± 9.1
Self home measurements			
Systolic	120.9 ± 12	129.2 ± 8.6	114.6 ± 11
Diastolic	74.8 ± 8.6	79.6 ± 7.1	71.2 ± 8
Ambulatory measurements 24 h			
Systolic	124.8 ± 10.2	133.8 ± 6.4	117.9 ± 6.7
Diastolic	68.3 ± 7.3	70.7 ± 7.2	66.5 ± 6.9
Daytime			
Systolic	126 ± 10.3	134.5 ± 7.5	119.6 ± 7.1
Diastolic	69.6 ± 7.8	71.6 ± 7.7	68.1 ± 7.1
Overnight			
Systolic	116.4 ± 14.7	129.9 ± 10.6	106.4 ± 7.6
Diastolic	61.7 ± 8	65.9 ± 7.1	57.4 ± 6.5

Correlation analyses were performed between ABPM results and home measurements. Statistically significant and moderate correlation was observed between mean systolic blood pressure measured by ABPM and mean home measurement of systolic blood pressure performed by the patients in the total group (r = 0.67; p = .001 for 24-h average, r = 0.62; p = .001 for daytime average, and r = 0.64; p = .001 for overnight measurements). On the other hand, although there was a weak but significant correlation between home measurements and ABMP regarding 24 hours systolic blood pressure, no statistically significant correlation between daytime or overnight systolic blood pressure measurements of ABPM and home records within the masked hypertension group (r = 0.33; p = .027, 24-h systolic blood pressures; r = 0.27; p = 0.067 daytime systolic blood pressure, r = 0.24; p = .11 overnight systolic blood pressure, for masked hypertension, respectively).

For cognitive assessment MMSE, MOCA, QMCI-TR, clock drawing test, trail making A, forward and backward digit span test, and categorical fluency test were performed to all patients. Median MMSE scores were significantly lower in masked hypertension group (28 [18–30] vs 29 [18–30], respectively, p = .011). Mean MOCA scores were lower in masked hypertension group, but this difference was not significant (16.4 ± 5.6 vs 18.5 ± 5.6, respectively, p = .07). Mean QMCI-TR scores were significantly lower in masked hypertension group (41.4 ± 12.9 vs 47.19 ± 15.1, respectively, p = .046). Categorical fluency test scores were also significantly lower in masked hypertension group (14.3 ± 4.2 vs 16.7 ± 3.96, p = .004; respectively). No differences in clock drawing test, trail making A, forward, and backward digit span test scores were observed between masked hypertension and normotensive group.

To determine the factors affecting cognitive assessment test scores, after unadjusted analyses testing the association between masked hypertension and test scores, adjusted regression analyses were performed. The results of the unadjusted and adjusted models are shown in Table 3. Adjusted model regression analyses results showed that masked hypertension was the independent correlate for MMSE and categorical fluency test scores.

Discussion

The results of this study revealed that masked hypertension is present in 43% of the geriatric patients enrolled. One of the striking results was that MMSE, QMCI-TR, and categorical fluency test scores were significantly lower in masked hypertension group than the normotensive group. According to the results of this study, we can say that masked hypertension is not rare in this study population, and it is associated with cognitive functions in geriatric age group. As far as we know this is the first study that evaluates the association between masked hypertension and cognitive function in geriatric population. Therefore, this brings new information to the literature.

In the older age group, there are large cohort studies evaluating the prevalence of masked hypertension. Different studies have reported different rates, ranging from 7 to 40% (2,35–37). A Spanish cohort study, in which hypertensive patients were not excluded, 7% had masked hypertension (35). Another study found the prevalence of masked hypertension to be 9% in 5000 older adults treated for hypertension (36). In a study examining previously untreated geriatric patients the prevalence was 40% (2). The result of our study is consistent with the latter study. The novelty of our study is excluding patients with hypertension and patients receiving any antihypertensive treatment unlike other studies in the literature.

Our study shows that masked hypertension has a negative influence on cognitive functions. This result supports the vascular risk factors hypothesis in the pathogenesis of cognitive dysfunction. Vascular risk factors including hypertension, diabetes mellitus, dyslipidemia, coronary artery disease, endothelial dysfunction, and smoking increase the risk of Alzheimer's Disease (5,38–41). In longitudinal follow-up studies, controlling hypertension was shown to decrease the risk of cognitive dysfunction and dementia (6,42–45). In the light of these studies, it can be concluded that high blood pressure, especially beginning from the middle age, is associated with cognitive dysfunction and increases the risk of dementia and Alzheimer's Disease. Likewise, the resemblance of pathologic findings in hypertensive and demented patients in autopsy series give evidence regarding the link between hypertension and cognitive dysfunction. The results of our study points out that, the negative influence of high blood pressure on cognitive functions may begin at masked hypertension stage, even before the level of apparent hypertension.

In a study examining the relationship between ABPM and cognitive functions, patients aged over 60 years were included and an association was found between blood pressure regulation and cognitive functions (46). Ninety-one patients who were over 60 years were included in this study while all patients were 65 years and over in our study. In the mentioned study in which hypertensive patients were included, Geriatric Depression Scale and MMSE scores were compared between the groups dipper/non-dipper and regulated/non-regulated blood pressure. Although no difference was observed between the groups dipper–nondipper; positive correlation was observed between regulated blood pressure and MMSE scores. In our study, as the effect of hypertension on cognitive function is already known, we excluded patients with hypertension. Therefore, we could examine the effect of masked hypertension on cognitive function, which is new in the literature. To the best of our knowledge, this present study is the first study highlighting the relationship between masked hypertension and cognitive functions.

Besides the effect of hypertension causing risk for cognitive decline, hypotension also causes cognitive dysfunction by reducing cerebral perfusion (31,32). This shows that blood pressure of older age should be within normal limits. In a study performed by Sabayan *et al.*, positive correlation was observed between MMSE test scores and high blood pressure in older adults (47). A similar study conducted by Kuyumcu *et al.*, found that the prevalence

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Table 3. Unadjusted and Adjusted Multivariable Linear Regression Analyses Results for Factors Affecting Cognitive Assessment Test Scores

	MMSE	MOCA	QMCI-TR	Clock Drawing	Trail Making A	Forward Digit Span	Backward Digit Span	Categorical Fluency
Beta (95% Confidence Interval)								
Model 1								
Masked hypertension	−0.247	−0.179	−0.198	−0.11	0.109	−0.028	−0.118	−0.283
	(−2.46, −0.31)*	(−4.32, 0.18)	(−11.41, −0.11)*	(−0.97, 0.27)	(−3.72, 11.48)	(−0.72, 0.54)	(−1.05, 0.26)	(−4.03, −0.79)**
Model 2								
Masked hypertension	−0.186	−0.054	−0.07	−0.27	0.051	0.077	−0.008	−0.196
	(−2.08, −0.003)*	(−2.23, 0.99)	(−6.51, 2.42)	(−0.61, 0.44)	(−5.01, 8.62)	(−0.29, 0.79)	(−0.53, 0.48)	(−3.15, −0.18)*
Age	−0.077	−0.18	−0.244	0.002	0.12	−0.094	−0.109	−0.273
	(−0.13, 0.05)	(−0.32, −0.04)**	(−1.004, −0.229)**	(−0.04, 0.05)	(−0.23, 1.01)	(−0.073, 0.02)	(−0.08, 0.01)	(−0.33, −0.07)**
Sex	0.018	0.013	−0.103	0.024	−0.023	−0.146	0.024	0.042
(Female)	(−0.99, 1.19)	(−1.54, 1.84)	(−7.699, 1.66)	(−0.47, 0.62)	(−7.77, 6.16)	(−1.04, 0.09)	(−0.45, 0.61)	(−1.19, 1.92)
Education	0.341	0.685	0.605	0.581	−0.485	0.588	0.651	0.337
	(0.29, 1.08)**	(2.24, 3.46)***	(4.67, 8.04)***	(0.46, 0.86)***	(−8.91, −3.74)***	(0.47, 0.88)***	(0.59, 0.97)***	(0.47, 1.59)***
Model 3								
Masked hypertension	−0.185	−0.052	−0.06	−0.013	0.079	0.105	−0.034	−0.194
	(−2.1, 0.02)*	(−2.27,1.06)	(−6.31, 2.84)	(0.58, 0.49)	(−4.16,9.78)	(−0.21, 0.88)	(−0.61, 0.39)	(−3.1, −0.15)*
Age	−0.093	−0.197	−0.268	−0.001	0.114	−0.106	−0.129	−0.297
	(−0.14, 0.05)	(−0.34, −0.05)**	(−1.08, −0.27)**	(−0.05,0.05)	(−0.27, 1.0)	(−0.8, 0.2)	(−0.08,0.007)	(−0.35, −0.08)**
Sex	0.033	0.031	−0.062	0.020	0.004	−0.131	0.059	0.091
(female)	(−0.98, 1.36)	(−1.47, 2.19)	(−6.86,3.21)	(−0.53, 0.65)	(−7.55, 7.8)	(−1.02,0.19)	(−0.35,0.75)	(−0.87,2.43)
Education	0.333	0.688	0.633	0.582	−0.442	0.608	0.655	0.364
	(0.26, 1.08)**	(2.22, 3.5)***	(4.87,8.4)***	(0.45, 0.87)***	(−8.46, −3.04)***	(0.49, 0.91)***	(0.59,0.98)***	(0.54,1.69)***
Smoking	−0.067	−0.021	−0.097	−0.045	−0.148	−0.149	0.073	−0.109
	(−0.94, 0.48)	(−1.26, 0.96)	(−4.8, 1.31)	(−0.45, 0.27)	(−7.93, 1.48)	(−0.66,0.07)	(−0.18,0.48)	(−1.57,0.43)
Depression	0.094	0.043	0.044	−0.069	−0.072	−0.082	0.201	0.139
	(−0.69, 1.98)	(−1.48, 2.7)	(−4.19, 7.33)	(−0.94,0.41)	(−12.1, 5.8)	(−1.01,0.37)	(0.19,1.44)*	(−0.44,33.3)
Diabetes mellitus	−0.073	−0.066	0.003	−0.097	0.050	−0.105	0.127	−0.105
	(−1.75, 0.76)	(−2.87, 1.05)	(−5.3, 5.5)	(−1.0, 0.26)	(−6.3, 10.66)	(−1.05, 0.24)	(−0.08,1.09)	(−1.05,0.24)
Alcohol consumption	0.093	−0.028	−0.031	−0.032	−0.032	−0.027	0.017	−0.027
	(−0.89, 2.5)	(−3.16, 2.15)	(−8.71, 5.94)	(−1.01, 0.7)	(−11.9,8.7)	(−1.01, 0.75)	(−0.71, 0.88)	(−1.01,0.75)

Note. Model 1 = unadjusted; Model 2 = Model 1+ age, sex, and education; Model 3 = Model 2 + alcohol consumption, smoking, depression, and diabetes mellitus. MMSE = Mini-Mental State Examination test; MOCA = Montreal Cognitive Assessment Scale; QMCI = Quick Mild Cognitive Impairment Test.

*$p < .05$, **$p < .01$, ***$p < .001$.

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of hypertension was lower in patients with Alzheimer's Disease compared to controls (60.6 vs 70.5%, $p = .005$) (6). As a result of subgroup analysis of 96 patients aged 85 years and over, high blood pressure was not related to cognitive decline in this age group (34). Although it may seem that the results of our study are not consistent with these studies, the difference in results may be due to the different methodology of these studies. The mean age of our study population was lower and there were only 10 patients aged 85 and over. Furthermore, the cognitive assessment of our study was more comprehensive and a variety of cognitive assessment tests were performed in addition to MMSE. Patients with masked hypertension scored lower in MMSE, MOCA, QMCI-TR, and categorical fluency tests. However, MOCA was of borderline significance, and in adjusted analyses MOCA and QMCI-TR were not significantly associated with masked hypertension. This may be due to the sample size of our study. It may be possible that further studies with larger samples may show a meaningful difference between these scores. In order to determine whether masked hypertension increases the risk of dementia, or whether treatment of masked hypertension has positive or negative influence on cognitive functions, long-term follow-up studies are needed.

Masked hypertension can be diagnosed by performing a correct home measurement as well as ABPM (24). Although, ambulatory blood pressure measurements were not correlated with home measurements in the masked hypertension group in our study. For diagnosing hypertension correctly based on home measurements, performing 12–14 measurements in the morning and evening is recommended for a week (38,48). Several studies show that home measurements were similar to 24 hours ABPM results but had differences from office measurements (38). All patients were asked to perform home measurements in our study. However, not all of them could adhere to the recommendations regarding home measurements. Home measurements were lower than ABPM in masked hypertension group. This shows that if we rely on home measurements, masked hypertension can be underdiagnosed. Home measurements may not be enough and reliable in geriatric population. These results underline the importance of the role of ABPM in the diagnosis of hypertension in geriatric population.

As this is a cross-sectional study, causality and long-term effects of masked hypertension on cognition could not be assessed. Longitudinal follow-up studies are needed to determine the effect of masked hypertension on progression of cognitive dysfunction and the incidence of dementia. Sample size can also be noted as a limitation. Further studies with larger number of patients with different ethnicity and race may be more effective to elucidate this relationship more accurately and to generalize the results. Another limitation is that ABPM could not be installed to morbid obese patients because of the cuff diameter. If morbid obese patients could have been analyzed, it is possible that the frequency of masked hypertension would have been determined higher. Long-term studies are needed to determine whether treatment is necessary or not in patients with masked hypertension, to evaluate the effects of treatment of masked hypertension on cognitive functions.

Conclusion

Masked hypertension is not rare in geriatric age group. This is an entity that should not be overlooked in geriatric medicine outpatient clinics. The results of our study show that masked hypertension is associated with cognitive functions. Cognitive assessment is essential in patients with masked hypertension. Performing cognitive tests sensitive to early and mild cognitive impairment will give clinicians a chance to diagnose cognitive dysfunction at early stage.

Conflict of interest

None.

References

1. Pickering TG, Davidson K, Gerin W, Schwartz JE. Masked hypertension. *Hypertension*. 2002;40:795–796. doi:10.1161/01.HYP.0000038733.08436.98
2. Mallion JM, Clerson P, Bobrie G, Genes N, Vaisse B, Chatellier G. Predictive factors for masked hypertension within a population of controlled hypertensives. *J Hypertens*. 2006;24:2365–2370. doi:10.1097/01.hjh.0000251895.55249.82
3. Pierdomenico SD, Cuccurullo F. Prognostic value of white-coat and masked hypertension diagnosed by ambulatory monitoring in initially untreated subjects: an updated meta analysis. *Am J Hypertens*. 2011;24:52–58. doi:10.1038/ajh.2010.203
4. Hänninen MR, Niiranen TJ, Puukka PJ, Kesäniemi YA, Kähönen M, Jula AM. Target organ damage and masked hypertension in the general population: the Finn-Home study. *J Hypertens*. 2013;31:1136–1143. doi:10.1097/HJH.0b013e32835fa5dc
5. Mancia G, Sega R, Bravi C, et al. Ambulatory blood pressure normality: results from the PAMELA study. *J Hypertens*. 1995;13:1377–1390.
6. Kuyumcu ME, Yesil Y, Oztürk ZA, et al. Alzheimer's disease is associated with a low prevalence of hypertension. *Dement Geriatr Cogn Disord*. 2012;33:6–10. doi:10.1159/000336053
7. Prince MJ, Bird AS, Blizard RA, Mann AH. Is the cognitive function of older patients affected by antihypertensive treatment? Results from 54 months of the Medical Research Council's trial of hypertension in older adults. *BMJ*. 1996;312:801–805. doi:10.1136/bmj.312.7034.801
8. Starr JM, Whalley LJ, Deary IJ. The effects of antihypertensive treatment on cognitive function: results from the HOPE study. *J Am Geriatr Soc*. 1996;44:411–415. doi:10.1111/j.1532-5415.1996.tb06412.x
9. Collaborative P, Neal B, MacMahon S. Effects of blood pressure lowering with perindopril and indapamide therapy on dementia and cognitive decline in patients with cerebrovascular disease. *Arch Intern Med*. 2003;163:1069–1075. doi:10.1001/archinte.163.9.1069
10. Peters R, Beckett N, Forette F, et al.; HYVET investigators. Incident dementia and blood pressure lowering in the Hypertension in the Very Elderly Trial cognitive function assessment (HYVET-COG): a double-blind, placebo controlled trial. *Lancet Neurol*. 2008;7:683–689. doi:10.1016/S1474-4422(08)70143-1
11. Weber MA. The effects on dementia of long-term treatment of hypertension. *Rev Cardiovasc Med*. 2003;4:197–198.
12. Goldstein FC, Hajjar IM, Dunn CB, et al. The relationship between cognitive functioning and the JNC-8 guidelines for hypertension in older adults. *J Gerontol A Biol Sci Med Sci*. 2016;glw181.
13. Guo Z, Viitanen M, Fratiglioni L, Winblad B. Low blood pressure and dementia in elderly people: the Kungsholmen project. *BMJ*. 1996;312:805–808. doi:10.1136/bmj.312.7034.805
14. Launer LJ, Masaki K, Petrovitch H, Foley D, Havlik RJ. The association between midlife blood pressure levels and late-life cognitive function. The Honolulu-Asia Aging Study. *JAMA*. 1995;274:1846–1851. doi:10.1001/jama.1995.03530230032026
15. Lurbe E, Torro I, Alvarez V, et al. Prevalence, persistence, and clinical significance of masked hypertension in youth. *Hypertension*. 2005;45:493–498. doi:10.1161/01.HYP.0000160320.39303.ab
16. Ateş İ, Altay M, Kaplan M, et al. Relationship between socioeconomic level, and the prevalence of masked hypertension and asymptomatic organ damage. *Med Sci Monit*. 2015;21:1022–1030. doi:10.12659/MSM.892684
17. Liu JE, Roman MJ, Pini R, Schwartz JE, Pickering TG, Devereux RB. Cardiac and arterial target organ damage in adults with elevated ambulatory

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and normal office blood pressure. *Ann Intern Med*. 1999;131:564–572. doi:10.7326/0003-4819-131-8-199910190-00038

18. Fan HQ, Li Y, Thijs L, et al.; International Database on Ambulatory Blood Pressure In Relation to Cardiovascular Outcomes Investigators. Prognostic value of isolated nocturnal hypertension on ambulatory measurement in 8711 individuals from 10 populations. *J Hypertens*. 2010;28:2036–2045. doi:10.1097/HJH.0b013e32833b49fe
19. Franklin SS, Thijs L, Li Y, et al. Masked hypertension in diabetes mellitus. *Hypertension*. 2013; 61:964–971. doi:10.1161/HYPERTENSIONAHA.111.00289
20. Salles GF, Leite NC, Pereira BB, Nascimento EM, Cardoso CR. Prognostic impact of clinic and ambulatory blood pressure components in high-risk type 2 diabetic patients: the Rio de Janeiro Type 2 Diabetes Cohort Study. *J Hypertens*. 2013;31:2176–2186. doi:10.1097/HJH.0b013e328364103f
21. Boggia J, Li Y, Thijs L, et al. Prognostic accuracy of day versus night ambulatory blood pressure: a cohort study. *Lancet*. 2007;370:1219–1229. doi:10.1016/S0140-6736(07)61538-4
22. Arik G, Varan HD, Yavuz BB, et al. Validation of Katz index of independence in activities of daily living in Turkish older adults. *Arch Gerontol Geriatr*. 2015;61:344–350. doi:10.1016/j.archger.2015.08.019
23. Guigoz Y, Lauque S, Vellas BJ. Identifying the elderly at risk for malnutrition. The Mini Nutritional Assessment. *Clin Geriatr Med*. 2002;18:737–757.
24. Sarikaya D, Halil M, Kuyumcu ME, et al. Mini nutritional assessment test long and short form are valid screening tools in Turkish older adults. *Arch Gerontol Geriatr*. 2015;61:56–60. doi:10.1016/j.archger.2015.04.006
25. Brink TL, Yesavage JA, Lum O, et al. Screening tests for geriatric depression. *Clin Gerontol*. 1982;1:37–43.
26. Stähelin HB, Monsch AU, Spiegel R. Early diagnosis of dementia via a two-step screening and diagnostic procedure. *Int Psychogeriatr*. 1997;9 Suppl 1:123–130.
27. 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.
28. Kaya Y, Aki OE, Can UA, Derle E, Kibaroğlu S, Barak A. Validation of montreal cognitive assessment and discriminant power of montreal cognitive assessment subtests in patients with mild cognitive impairment and alzheimer dementia in Turkish Population. *J Geriatr Psychiatry Neurol*. 2014;27:103–109. doi:10.1177/0891988714522701.
29. Yavuz BB, Varan HD, O'Caoimh R, et al. Validation of the Turkish version of the quick mild cognitive impairment screen. *Am J Alzheimers Dis Other Demen*. 2017;32:145–156. doi:10.1177/1533317517691122
30. Urbina EM, Williams RV, Alpert BS, et al.; American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee of the Council on Cardiovascular Disease in the Young. Noninvasive assessment of subclinical atherosclerosis in children and adolescents: recommendations for standard assessment for clinical research: a scientific statement from the American Heart Association. *Hypertension*. 2009;54:919–950. doi:10.1161/HYPERTENSIONAHA.109.192639
31. Head GA, Mihailidou AS, Duggan KA, et al.; Ambulatory Blood Pressure Working Group of the High Blood Pressure Research Council of Australia. Definition of ambulatory blood pressure targets for diagnosis and treatment of hypertension in relation to clinic blood pressure: prospective cohort study. *BMJ*. 2010;340:c1104. doi:10.1136/bmj.c1104
32. O'Brien E, Asmar R, Beilin L, et al.; European Society of Hypertension Working Group on Blood Pressure Monitoring. Practice guidelines of the European Society of Hypertension for clinic, ambulatory and self blood pressure measurement. *J Hypertens*. 2005;23:697–701.
33. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Blood Pressure*. 2013;22:193–278. doi:10.3109/08037051.2013.812549
34. Staessen JA, Fagard RH, Lijnen PJ, Thijs L, Van Hoof R, Amery AK. Mean and range of the ambulatory pressure in normotensive subjects from a meta-analysis of 23 studies. *Am J Cardiol*. 1991;67:723–727.
35. Banegas JR, de la Cruz JJ, Graciani A, et al. Impact of ambulatory blood pressure monitoring on reclassification of hypertension prevalence and control in older people in Spain. *J Clin Hypertens (Greenwich)*. 2015;17:453–461. doi:10.1111/jch.12525
36. Bobrie G, Chatellier G, Genes N, et al. Cardiovascular prognosis of "masked hypertension" detected by blood pressure self-measurement in elderly treated hypertensive patients. *JAMA*. 2004;291:1342–1349. doi:10.1001/jama.291.11.1342
37. Gijón-Conde T, Graciani A, López-García E, et al. Short-term variability and nocturnal decline in ambulatory blood pressure in normotension, white-coat hypertension, masked hypertension and sustained hypertension: a population-based study of older individuals in Spain. *Hypertens Res*. 2017;40:613–619. doi:10.1038/hr.2017.9
38. Verberk WJ, Kroon AA, Kessels AG, de Leeuw PW. Home blood pressure measurement: a systematic review. *J Am Coll Cardiol*. 2005;46:743–751. doi:10.1016/j.jacc.2005.05.058
39. Dede DS, Yavuz B, Yavuz BB, et al. Assessment of endothelial function in Alzheimer's disease: is Alzheimer's disease a vascular disease? *J Am Geriatr Soc*. 2007;55:1613–1617. doi:10.1111/j.1532-5415.2007.01378.x
40. Sparks DL, Scheff SW, Liu H, Landers TM, Coyne CM, Hunsaker JC 3rd. Increased incidence of neurofibrillary tangles (NFT) in non-demented individuals with hypertension. *J Neurol Sci*. 1995;131:162–169. doi:10.1016/0022-510X(95)00105-B
41. Palta P, Carlson MC, Crum RM, et al. Diabetes and cognitive decline in older adults: the Ginkgo evaluation of memory study. *J Gerontol A*. glx076. doi:10.1093/gerona/glx076.
42. Drawz PE, Alper AB, Anderson AH, et al. Masked hypertension and elevated nighttime blood pressure in CKD: prevalence and association with target organ damage. *Clin J Am Soc Nephrol*. 2016;11:642–52. doi:10.2215/CJN.08530815
43. Unsal S, Ozkara A, Albayrak T, et al. Evaluation of prehypertension and masked hypertension rate among clinically normotensive patients. *Clin Exp Hypertens*. 2016:1–7. doi:10.3109/10641963.2015.1047951
44. Forette F, Seux ML, Staessen JA, et al.; Systolic Hypertension in Europe Investigators. The prevention of dementia with antihypertensive treatment: new evidence from the Systolic Hypertension in Europe (Syst-Eur) study. *Arch Intern Med*. 2002;162:2046–2052. doi:10.1001/archinte.162.18.2046
45. Hajjar I, Catoe H, Sixta S, et al. Cross-sectional and longitudinal association between antihypertensive medications and cognitive impairment in an elderly population. *J Gerontol A Biol Sci Med Sci*. 2005;60:67–73.
46. Savan DK, Cengiz M, Yavuzer H, et al. Relation of ambulatory blood pressure measurement and cognitive functions in hypertensive elderly patients. *Aging Clin Exp Res*. 2015:1–6. doi:10.1007/s40520-015-0477-2
47. Sabayan B, Oleksik AM, Maier AB, et al. High blood pressure and resilience to physical and cognitive decline in the oldest old: the Leiden 85-plus Study. *J Am Geriatr Soc*. 2012;60:2014–2019. doi:10.1111/j.1532-5415.2012.04203.x
48. Andersen MJ, Khawandi W, Agarwal R. Home blood pressure monitoring in CKD. *Am J Kidney Dis*. 2005;45:994–1001. doi:10.1053/j.ajkd.2005.02.015

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