Research Paper

The study of antecedent clinical manifestations of hypertensive heart disease in cohort of hypertension

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ABSTRACT

Hypertensive heart disease presents increasing morbidity and mortality worldwide, however, the data about its epidemics and its specific symptoms in hypertension patients is scarce. To assess the frequency and correlated symptoms of hypertensive heart disease, 800 hypertension patients were randomly recruited for this study per the guidelines of the American College of Cardiology. The diagnosis of heart disease and its typical symptoms (palpitation and angina) were analyzed for the frequency of hypertensive heart disease in hypertension cohort. Cross-tabulation analysis was used to study the correlation between psychiatric indexes (annoy, amnesia, irritableness, depression, anxiety, and fear) and palpitation, the correlation between physical disorders (backache, lumbar debility, and numbness of limbs) and palpitation, and the correlation between symptoms (dizziness, daze, headache, and tinnitus) and palpitation presented in hypertensive patients. It was found that around half of patients suffered hypertensive heart disease, which correlated to certain physical and mental symptoms. Significant correlation exists between palpitation and annoy / amnesia. Significant correlation exists between palpitation and backache / lumbar debility / numbness of limbs; and significant correlation exists between palpitation and dizziness / daze / headache / tinnitus. These results provide clinical insights into the modifiable antecedent clinical conditions which are risk factors for hypertensive heart disease in elderly and will help improve early management of this disease.

INTRODUCTION

Complications caused by hypertension have been a prevalent public health issue, further, the cardiac complications are the main cause of morbidity and mortality in the patients with high blood pressure [1, 2]. The first definition of hypertensive heart disease (HHD) was proposed in 1979 by the New York Heart Association, which defined HHD as an anatomo-functional alteration characterized by left ventricular hypertrophy (LVH) and cardiac failure in patients with systemic hypertension [3]. In 1992, Frohlich et al. defined HHD as the response of myocardium to the afterload imposed by increased blood pressure that leads to LVH [4]. However, the comprehensive definition of HHD could be a complex and variable syndrome including clinical manifestations derived from LVH, myocardial ischemia and rhythm abnormalities (arrhythmia), which are obviously related to each other and all of which can be resulted from the effects of high blood pressure on the heart [5–7].

Age may be the paramount risk factor for HHD, but superimposed on age are modifiable antecedent clinical conditions, the first of which is hypertension [8–12]. Therefore, preventing hypertension is an effective preventive measure to decrease HHD prevalence in elderly. Indeed, hypertension has already been a major public health issue with a remarkable morbidity, and the prevalence of hypertension has reached alarming proportions worldwide with rapid economic development and lifestyle changes [13]. It was estimated that 30% of population worldwide would suffer hypertension within next decade [14, 15]. Hypertension has been known as a strong risk factor for heart disease, potentially lethal ventricular arrhythmias and sudden cardiac death occurred more common in hypertensive patients than others [16]. Existing studies on hypertension symptoms focused on the relationship between symptoms and quality of life [17], the associations of symptom relief and treatments [18, 19], and the symptom differentiations of normotensives, borderline hypertensives and hypertensives [20]. To our knowledge, no studies have investigated the correlations among different symptoms of hypertension and the correlations between each symptom and HHD. Such study is not only interesting, but also of great clinical significance. A variety of symptoms may be directly or indirectly related to hypertension, such as dizziness, nervousness, sweating, sleep disorder, facial flushing, and blood spots in the eyes, etc. Some of those symptoms might not only be caused by high blood pressure but also caused by hypertension involved heart diseases. The MAYO CLINIC has outlined some symptoms from HHD. Chest pain, chest tightness and angina could be main clinical manifestation of heart diseases originated from hypertension, also shortness of breath, dizziness, pain in the neck, pain in the back, pain or numbness in the limbs are often seen in patients with HHD. However, persistent cough, swelling in legs, hands, ankles or feet more likely result from heart diseases originated from cardiomyopathy or heart infection and heart defects. Exploring the correlations of distinct symptoms and HHD could be interesting and meaningful. In addition, although higher than normal blood pressures can be objectively measured, symptom observation plays an indispensable role because eventually, we treat the symptoms as well as the underlying conditions but not the numbers. Therefore, statistically studying the prevalence of each symptom and the correlations among each symptom based on a large population will provide important insight into cost-effective long-term hypertension management and HHD control.

Furthermore, although HHD is the number one cause of death associated with high blood pressure [21], original clinical studies on epidemics of HHD in hypertensive patients are still scarce. Díez found that hypertension increased the age-adjusted and risk-factor adjusted hazard of heart failure 2-fold in men and 3-fold in women [22]. However, heart failure and HHD are two distinct concepts. Ischemic heart disease, HHD, and aortic valve disease may all cause heart failure. Herweg et al. found that hypertension and HHD in patients are associated with pulmonary vein dilation but did not assess the epidemics of HHD in hypertensive patients [23]. Ekström et al. studied the transition from hypertension to HHD and heart failure in their PREFERS study [24]. However, the detailed correlation between HHD and hypertension symptoms is still unclear. Therefore, evaluation of both the HHD prevalence and the correlations between HHD and hypertension symptoms is in an urgent need, which may help establish a possibility that we could preidentify those hypertensive patients who are predisposed to developing HHD before the appearance of clinical manifestations and treat them with some preventive measures. To this end, we statistically analyzed the frequency of HHD and the correlations between HHD and selected symptoms in this study.

MATERIALS AND METHODS

Patients

All the 800 patients were randomly recruited from Qingdao, a metropolis in northeast China with a population of over 9 million people. Clinical data were collected at the Qingdao Fifth People's Hospital, the Shandong Qingdao Hospital of Integrated Traditional and Western Medicine, and their local community health centers and township central hospitals. All the patients were diagnosed with hypertension according to

"Hypertension Practice Guidelines in China". The patients were selected with the random gender, marriage, and level of educations. Patients' age ranged from 40 to 80 years old. Patients' hypertension history age ranged from 1 to 20 years with or without family medical history of hypertension. The exclusion criteria included poor compliance, severe medical condition, and pregnancy or breast-feeding.

Study design

All the patients were required to answer a questionnaire including medical history, family medical history, and lifestyle. The hypertension and its symptoms were diagnosed and assessed per ACC guidelines [25]. Cross-tabulation analysis was used to study the correlation between psychiatric indexes (annoy, amnesia, irritableness, depression, anxiety, and fear) and palpitation, the correlation between physical disorders (backache, lumbar debility, and numbness of limbs) and palpitation, and the correlation between high blood pressure symptoms (dizziness, daze, headache, and tinnitus) and palpitation presented in hypertensive patients. The blood routine examination was conducted for each patient.

Statistical analysis

Categorical data were compared using the Chi-square test. Continuous data were expressed as mean standard deviation and compared using the Student's t test (IBM SPSS Statistics 23). All *p*-values were two-tailed with the level of statistical significance set at 0.05.

RESULTS

The frequencies of patients suffering complicated cardiac disorders in hypertensive cohort

Eight hundred patients with hypertension were randomly selected and surveyed. We found that 46.38% of patients had slight palpitation, 4.63% of patients had medium palpitation, and 0.13% of patients had severe palpitation (Figure 1A and Supplementary Table 1). We found that

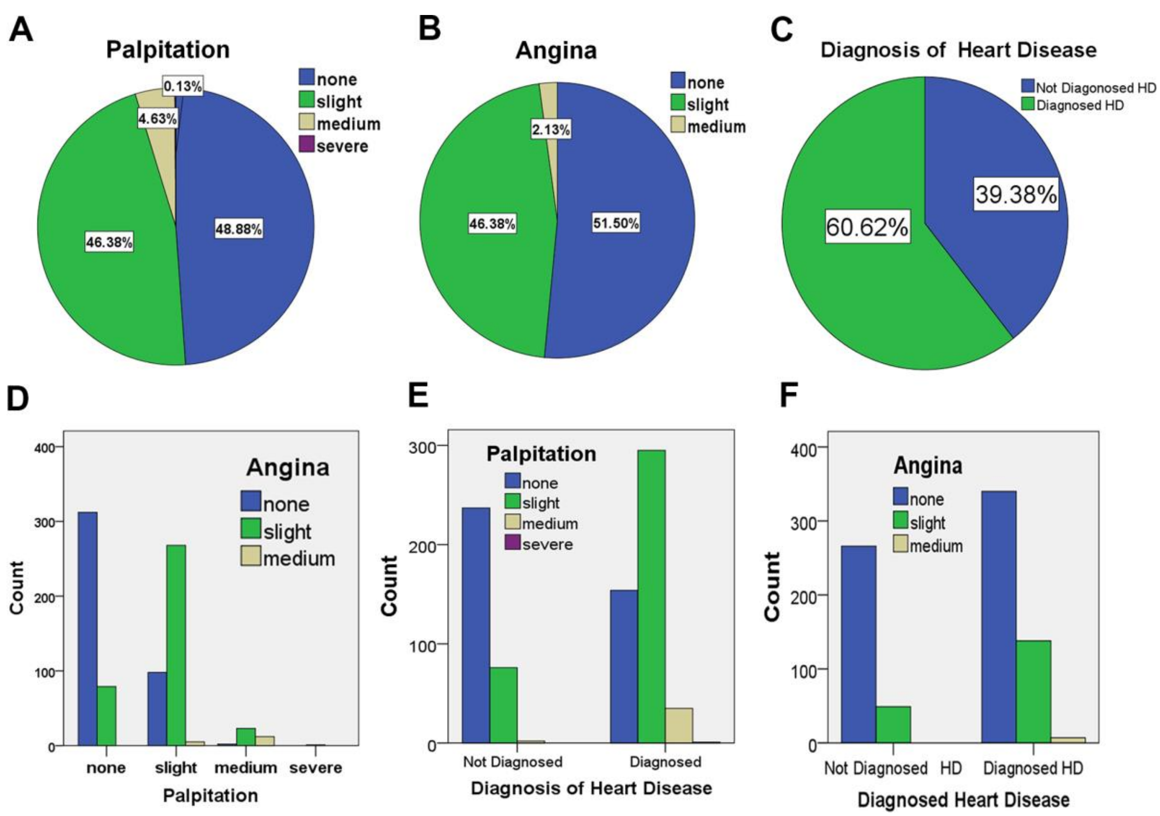

Figure 1. The percentages of patients with cardiac disorders in hypertensive cohort. The data was collected and analyzed from 800 cases of hypertension in northern China (n = 800). (**A**). The percentages of patients with different levels of palpitation in all patients with hypertension. (**B**). The percentages of patients with different levels of angina in all patients with hypertension. (**C**). The percentages of patients with diagnosis of heart disease in all patients with hypertension. (**D**). The analysis of cross-classification of palpitation and angina pectoris as corelated symptoms in patients with hypertension. (**E**). The analysis of cross-classification of palpitation and diagnosis of heart disease. (**F**). The analysis of cross-classification of Angina and diagnosis of heart disease.

46.38% of patients had slight angina pectoris, 2.13% of patients had medium-level angina, and no patients had severe angina (Figure 1B and Supplementary Table 2). More importantly, the diagnosis of heart disease demonstrates that a high frequency of heart disease among all hypertensive subjects as 60.62% (Figure 1C). To analyze the possible correlation of diagnosed heart disease, palpitation and angina, the cross-tabulation was performed. The significant correlation was observed between patients with palpitation and patients with angina (Supplementary Table 3). Most of patients with palpitation also have the symptom of angina (Figure 1D). Further, both of palpitation and angina are significantly correlated with the diagnosis of heart disease, especially palpitation presented dominantly in patients diagnosed with heart disease (Table 1A–1D and Figure 1E, 1F). The findings indicated that more than half of hypertensive patients in this study have complicating cardiac disease, and most of them shared both symptoms of palpitation and angina pectoris, which could be the associative indexes for diagnosis of HHD in hypertensive patients.

The psychiatric indexes correlate with palpitation presented in hypertensive patients

To identify the interrelated factors in HHD, we first checked if the mental disorders are correlated with palpitation in hypertensive patients. Different psychiatric indexes were checked from 800 cases randomly selected. We found the patients suffering annoy or amnesia approximately presented in half of the cases, patients suffering slight or medium mental annoy accounted for 45.38% in total, and patients with slight or medium amnesia accounted for 59.57% in total. However, the patients who have mental issues as either irritableness, depression, anxiety, or fear accounted for less than 25% of patients (Figure 2A – 2F and Supplementary Table 4A–4F). The high incidence rates of annoy and amnesia drove us to check if any correlations existing between these 2 mental symptoms and cardiac palpitation. Cross-tabulation was performed for patients with palpitation and patients with annoy or amnesia. It was found that patients with palpitation are significantly associated with patients with annoy (Figure 2G and Supplementary Table 5A, 5B). 25 cases out of a total 37 cases with medium palpitation also presented the symptom of annoy (67.6%) and 233 cases out of a total 371 cases with slight palpitation also presented the symptom of annoy (62.8%). This was similar for amnesia, the palpitation is significantly associated with amnesia in all patients (Figure 2H and Supplementary Table 5C, 5D). 30 cases out of a total 37 cases with medium palpitation also presented the amnesia (81.1%), and 247 cases out of a total 371 cases with slight palpitation also presented either slight or medium amnesia (66.6%). All the data suggested a positive correlation exists between palpitation and annoy/amnesia presented in hypertensive patients.

The physical disorders correlate with palpitation presented in hypertensive patients

Roughly 46% - 89.2% of patients suffered physical discomforts. In particular, patients suffering slight or medium backache accounted for 46% in total; patients suffering slight or medium lumbar debility 57.26% in total; and patients suffering numbness of limbs 46% in total (Figure 3A–3C and Supplementary Table 6A–6C). To assess the correlation between these physical disorders and palpitation, we performed cross-tabulation for patients with palpitation and patients with backache, lumbar debility or numbness of limbs. It was found that patients with palpitation were significantly correlated with patients with either backache and lumbar debility, or numbness of limbs (Figure 3D, 3F and Supplementary Table 7A–7F). A total of 236 cases out of 371 cases with slight palpitation suffered the symptoms of backache (63.6%); a total of 263 cases out of the 371 cases suffered the symptoms of lumbar debility (70.9%); a total of 210 cases out of the 371 cases suffered the symptoms of numbness of limbs (56.6%). A total of 23 cases out of 37 cases with medium palpitation suffered the symptoms of lumbar debility (62.2%); a total of 33 cases out of 37 cases suffered the symptoms of numbness of limbs (89.2%). Only one patient with severe palpitation suffered all the symptoms (back pain, lumbar debility and numbness of limbs). These results implied that the hypertensive patients with combined palpitation are susceptible to body disorders. This evidence is helpful for primary screen over cardiac complications in hypertension cohort.

The symptoms of dizziness, being dazed, headache and tinnitus are correlated with palpitation presented in hypertensive patients

Eight hundred hypertensive patients suffered dizziness, dazed headache, or tinnitus. Among them, 60.7% of patients suffered occasionally slight or medium dizziness, 48.9% occasionally slight or intermediate daze, 48.8% headache, and 58.7% tinnitus (Figure 4A–4D and Supplementary Table 8A–8D). To assess the correlations between these symptoms and palpitation, we performed cross-tabulation for patients suffering palpitation and symptoms of dizziness, daze, headache, and tinnitus. It was found that palpitation is significantly correlated with symptoms of dizziness, daze, headache, or tinnitus (Figure 4E–4H and Supplementary Table 9A–9H). Among the 371 cases with slight palpitation, 295 cases (79.5%) suffered dizziness; 232 cases daze (62.5%), 258 cases (69.5%) headache, 263 cases (70.9%) tinnitus.

Table 1A. The analysis of cross-classification by diagnosis of heart disease * palpitation crosstabulation in patients with hypertension.

		Palpitation				Total
		None	Slight	Medium	Severe	
Diagnosed Heart Disease	Not Diagnosed HD	237	76	2	0	315
	Diagnosed HD	154	295	35	1	485
Total		391	371	37	1	800

Table 1B. Chi-square tests for diagnosis of heart disease * palpitation crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	147.879a	3	.000
Likelihood Ratio	156.550	3	.000
Linear-by-Linear Association	140.304	1	.000
N of Valid Cases	800		

a. 2 cells (25.0%) have expected count less than 5. The minimum expected count is.39.

Table 1C. The analysis of cross-classification by diagnosis of heart disease * angina crosstabulation in patients with hypertension.

		Angina			Total
		None	Slight	Medium	
Diagnosed Heart Disease	Not Diagnosed HD	266	49	0	315
	Diagnosed HD	340	138	7	485
Total		606	187	7	800

Table 1D. Chi-square tests for diagnosis of heart disease * angina crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	23.323a	2	.000
Likelihood Ratio	26.484	2	.000
Linear-by-Linear Association	23.111	1	.000
N of Valid Cases	800		

a. 2 cells (33.3%) have expected count less than 5. The minimum expected count is 2.76.

Among the 37 cases with medium palpitation, 35 cases (94.6%) suffered dizziness, 21 cases (56.8%) daze, 24 (64.9%) cases headache, and 25 cases (67.6%) tinnitus. These results suggested that dizziness, daze, headache, and tinnitus could be the signs of complicated heart disease in hypertensive patients.

The correlations between palpitation and blood routine indexes in hypertensive patients

Blood routine lab is important for its accessibility and informativeness in hypertension management. We analyzed the 10 common indexes in blood routine from randomly selected 800 patients with hypertension (Supplementary Table 10 and Figure 5A–5J) and statistically checked their correlations with cardiac palpitation by SPSS Statistics 23. We found there were significantly positive correlations between palpitation and either homocysteine, total cholesterol, creatinine or uric acid (Supplementary Table 11A–11D), and the significantly negative correlations between palpitation and either triglyceride or high-density lipoprotein (Supplementary Table 11E, 11F).

DISCUSSION

HHD refers to a group of disorders that includes heart failure, ischemic heart disease, and LVH. It is known

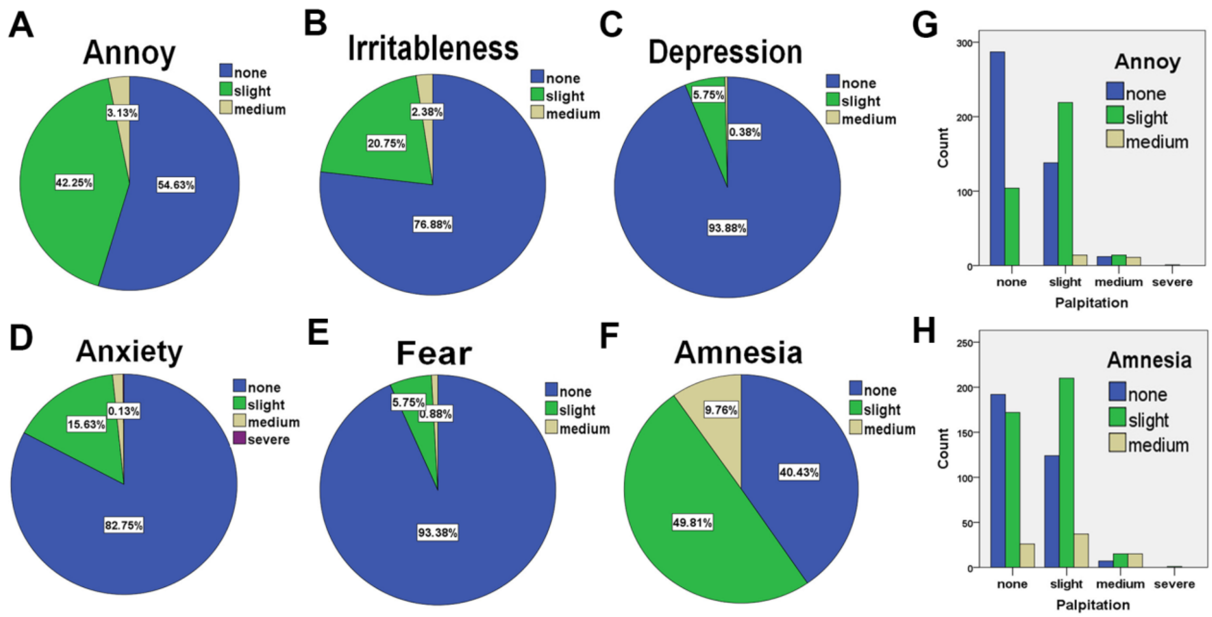

Figure 2. The frequencies of hypertensive patients suffering various mental symptoms and their correlations with palpitation (n = 800). (**A**) The percentages of patients who is annoyed with no reason. (**B**) The percentages of patients who are easy to get irritable. (**C**) The percentages of patients with depression. (**D**) The percentages of patients with anxiety. (**E**) The percentages of patients with fear. (**F**) The percentages of patients with amnesia. (**G**) The analysis of cross-classification of palpitation and psychiatric annoy in patients with hypertension. (**H**) The analysis of cross-classification of palpitation and psychiatric amnesia in patients with hypertension.

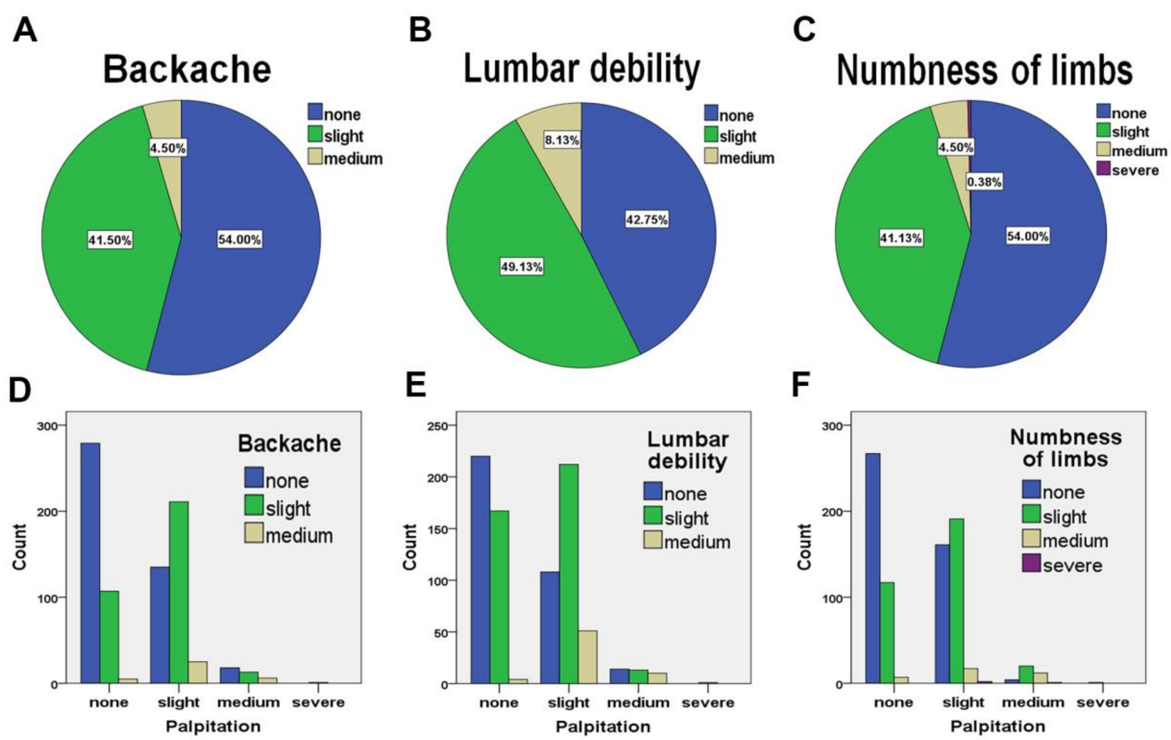

Figure 3. The frequencies of hypertensive patients suffering various physical symptoms and their correlations with palpitation (n = 800). The percentages of patients suffering backache (**A**), lumbar debility (**B**), and numbness of limbs (**C**). The analysis of cross-classification of palpitation and backache (**D**), palpitation and lumbar debility (**E**), and palpitation and numbness of limbs (**F**) in patients with hypertension.

that hypertension is a strong risk factor for heart disease, and HHD is the first cause of death associated with high blood pressure. Lethal ventricular arrhythmias and sudden cardiac death are more common in hypertensive patients than other types of heart diseases [16]. To initiate interventions as early as possible to prevent HHD from happening in hypertensive patients, it is necessary to assess the correlations between hypertension symptoms and HHD symptoms. To that end, we pooled the data from 800 hypertensive patients to systemically analyzed the correlation between the indexes of physical disorders, mental disorders, as well as

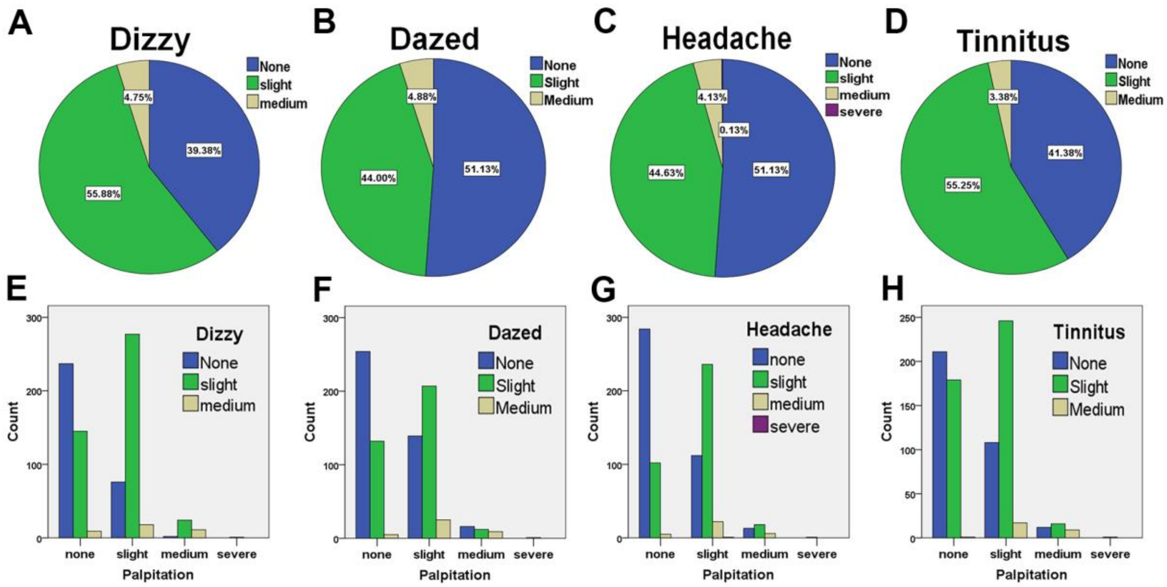

Figure 4. The frequencies of hypertensive patients suffering cephalic symptoms and their correlations with palpitation (n = 800). The percentages of patients suffering dizziness (**A**), daze (**B**), headache (**C**), and tinnitus (**D**). The analysis of cross-classification of palpitation and dizziness (**E**), palpitation and daze (**F**), palpitation and headache (**G**), and palpitation and tinnitus in patients with hypertension (**H**).

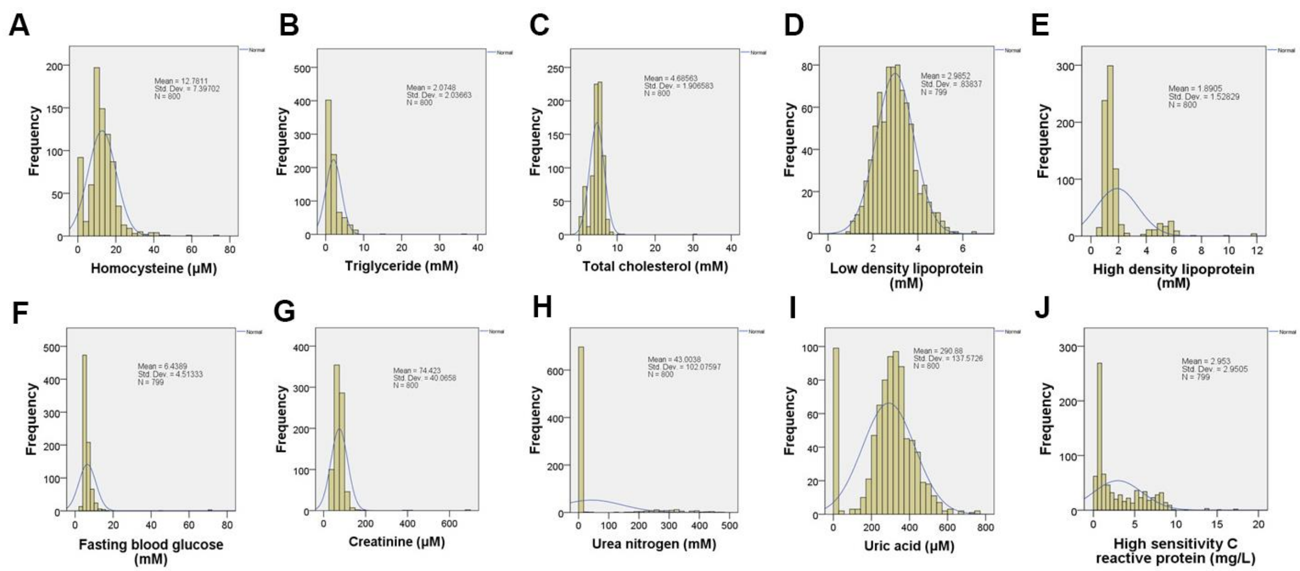

Figure 5. The examination of blood routine. The blood samples were collected and analyzed from hypertensive patients (n = 800). (**A**). Homocysteine; (**B**). Triglyceride; (**C**). Total cholesterol; (**D**). Low density lipoprotein; (**E**) High density lipoprotein; (**F**). Fasting blood glucose; (**G**). Creatinine; (**H**). Urea nitrogen; (**I**). Uric acid; (**J**). High sensitivity C reactive protein.

lab routine blood indexes and heart disease symptoms. Patients in our study are more female than male as 61.25% versus 38.75% and have hypertension history from 1 year to 20 years. 21.3% of patients had family hypertension history (Supplementary Figure 1; Supplementary Tables 12, 13). Approximately, half of patients, who were diagnosed as heart disease (Supplementary Figure 2), presented cardiac symptoms as palpitation or angina pectoris, more patients were at slight level and a few patients at medium level, which indicated a high incidence of complicated heart diseases. Our results are consistent with previous study. Weber et al. mentioned in his article that hypertension contributes importantly to increased risk of major cardiovascular events [14]. Jeremy Slivnick et al. believed that high blood pressure could lead to severe heart diseases such as LVH, which incitingly leads to diastolic dysfunction [26].

Regarding the epidemics of HHD, Lamprea-Montealegre et al. studied the prevalence of hypertension in the U.S., but not the prevalence of HHD in hypertensive patients. In addition, they only estimated the associated cardiovascular disease without any diagnosis [27]. The investigation by Nkoke et al. in Cameroon focused on the predominance of HHD among the allover patients with cardiac diseases but not in the basis of hypertensive patients [28]. To our knowledge, all of the previous studies focused on the prevalence of hypertension, but not on HHD [29]. In contrast, the current study first time systemically investigated the frequencies of HHD among a large population of hypertensive patients. Our data will provide insight into the prevention and intervention against HHD.

The hypertension is estimated to affect more than 600 million people worldwide [14], who are living with a high risk of heart disease. However, due to the asymptomatic or subclinical symptoms in early stage of HHD, many patients had already been an advanced HHD when they first presented to their primary care providers. This dramatically increases the damages caused by HHD such as asymptomatic LVH or LVH subclinical symptoms. Although electrocardiogram and echocardiogram are readily available to diagnose LVH, it will not be anticipated for the primary care providers to order those examinations for their patients without notable cardiac symptoms [16]. As the result, the late diagnoses always predispose those patients to a worse situation.

In this study, we considered the presence of the complex symptoms of patients including physical disorders and metal disorders instead of looking at only cardiac disorders. It’s very interesting, the correlations between cardiac palpitation and mental disorders (annoy and amnesia) were observed. Actually, the link between heart disease and brain health has been made aware of for recent years. It was observed that the abnormal blood flow might impair thinking ability. Chauvet-Gelinier and Bonin found that cardiac disorders impacted individual’s mental health [30]. Our study further assessed different indexes of mental conditions and found that only annoy and amnesia were significantly correlated to palpitation. Also, we found a close relationship between palpitation and some somatic disorders, such as backache, lumbar debility, numbness of limbs, and headache. Our results are consistent with previous study in this regard [31].

It is well known that age is the paramount risk factor for HHD. In this study, we took account of age by dividing patients into 4 groups of age, as years of 40-49, 50-59, 60-69 and more than 69. We found palpitation, which was considered as a representative clinical manifestation of heart disease, was significantly correlated with ages, but no significance was observed between angina and ages (Supplementary Table 14A–14D). These data demonstrate that age is a critical risk factor of HHD. Further, numbness of limbs, lumbar debility, backache, dazed head, headache, and tinnitus presented significance in correlation with ages. In contrast, amnesia, annoy, dizzy did not show significance in correlation with ages (Supplementary Table 14E–14V).

In summary, significant correlation exists between palpitation and angina. Significant correlation exists between palpitation and annoy / amnesia. Significant correlation exists between palpitation and backache / lumbar debility / numbness of limbs; and significant correlation exists between palpitation and dizziness / daze / headache / tinnitus. In addition, palpitation, numbness of limbs, lumbar debility, backache, dazed head, headache, and tinnitus were significantly correlated with age. These results provide clinical insights into early management of the modifiable antecedent clinical conditions. The success in management of these conditions will decrease HHD prevalence in elderly.

AUTHOR CONTRIBUTIONS

Conceptualization, Q. L., N. L., S.W., J.X. and X.Q.; Methodology, Q.L, N.L., and S.W.; Validation, J.X. and X.Q.; Formal Analysis, Q.L., N.L. and X.Q.; Investigation, Q.L., N.L., X.L., Y.L., L.C. and H.L.; Resources, Q.L., N.L. and S.W.; Writing-Original Draft, X.Q.; Writing-Review and Editing, S.W. and J.X.; Funding Acquisition, N.L.; Supervision, S.W., J.X. and X.Q. All authors have reviewed and agreed to this information.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

ETHICAL STATEMENT AND CONSENT

The study protocol was approved by the Institutional Review Boards (IRB) at Qingdao Fifth People's Hospital. IRB guidelines for conducting clinical research were strictly followed. The written consent was obtained from each subject prior enrollment in this study.

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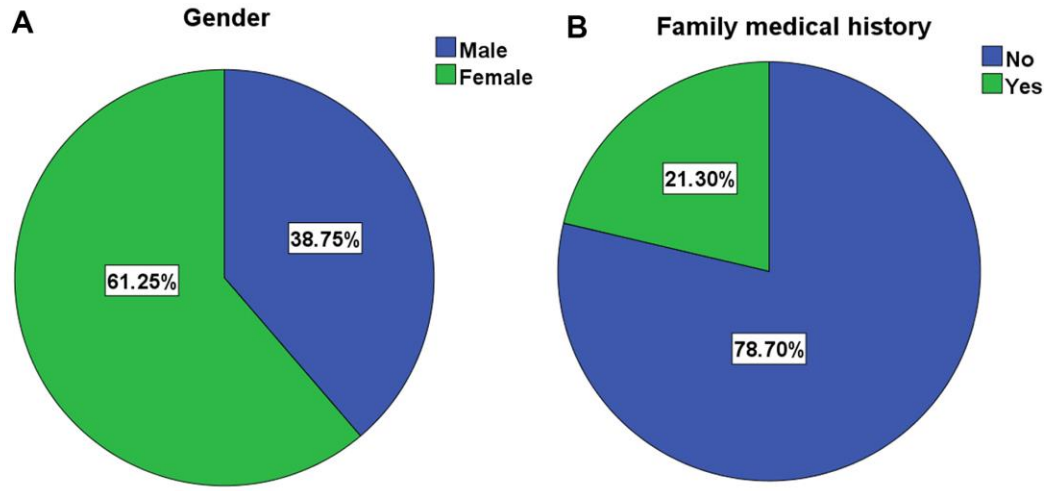
SUPPLEMENTARY MATERIALS

Supplementary Figures



Supplementary Figure 1. The distribution of hypertensive patients with different genders and family medical history. (**A**) The frequencies of male or female patients in total hypertensive patients. (**B**) The frequencies of patients with or without familial inheritance of hypertension.

Supplementary Figure 2. The representative echocardiogram images from hypertensive patients. Left: diagnosis as no obvious abnormality of cardiac structure was found. Right: diagnosis as Pulmonary regurgitation (mild); Aortic regurgitation (mild); Left ventricular diastolic dysfunction; Extended aortic and decreased aortic elasticity.

Supplementary Tables

Supplementary Table 1. The percentage of patients with palpitation.

		Frequency	Percent	Valid percent	Cumulative percent
Valid	**none**	391	48.9	48.9	48.9
	slight	371	46.4	46.4	95.3
	medium	37	4.6	4.6	99.9
	severe	1	.1	.1	100.0
	Total	800	100.0	100.0	

Note: "none" indicates no palpitation ever occurred with the patient; "slight" indicates less than 3 times palpitation occurred per day with the patient; "medium" indicates around 3-12 times palpitation occurred per day with the patient which doesn't delay patient's routine work; "severe" indicates palpitation occurred more than 12 times per day.

Supplementary Table 2. The percentage of patients with angina.

		Frequency	Percent	Valid percent	Cumulative percent
Valid	**none**	412	51.5	51.5	51.5
	slight	371	46.4	46.4	97.9
	medium	17	2.1	2.1	100.0
	Total	800	100.0	100.0	

Note: "none" indicates no angina ever occurred with the patient; "slight" indicates less than 3 times angina occurred per day with the patient; "medium" indicates around 3-12 times angina occurred per day with the patient which doesn't delay patient's routine work; "severe" indicates angina occurred more than 12 times per day with undermined living quality on patient.

Supplementary Table 3A. The analysis of cross-classification by palpitation * angina crosstabulation.

		Angina			Total
		None	**Slight**	**Medium**	
Palpitation	none	312	79	0	391
	slight	98	268	5	371
	medium	2	23	12	37
	severe	0	1	0	1
Total		412	371	17	800

Supplementary Table 3B. Chi-square tests for palpitation * angina crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	405.077[a]	6	.000
Likelihood Ratio	315.512	6	.000
Linear-by-Linear Association	270.656	1	.000
N of Valid Cases	800		

[a]4 cells (33.3%) have expected count less than 5. The minimum expected count is .02.

Supplementary Table 4A. The frequencies of patients who is annoyed with no reason.

		Frequency	Percent	Valid percent	Cumulative percent
Valid	none	437	54.6	54.6	54.6
	slight	338	42.3	42.3	96.9
	medium	25	3.1	3.1	100.0
	Total	800	100.0	100.0	

Supplementary Table 4B. The frequencies of patients with tendency to be irritable.

		Frequency	Percent	Valid percent	Cumulative percent
Valid	none	615	76.9	76.9	76.9
	slight	166	20.8	20.8	97.6
	medium	19	2.4	2.4	100.0
	Total	800	100.0	100.0	

Supplementary Table 4C. The frequencies of patients with depression.

		Frequency	Percent	Valid percent	Cumulative percent
Valid	none	751	93.9	93.9	93.9
	slight	46	5.8	5.8	99.6
	medium	3	.4	.4	100.0
	Total	800	100.0	100.0	

Supplementary Table 4D. The frequencies of patients with anxiety.

		Frequency	Percent	Valid percent	Cumulative percent
Valid	none	662	82.8	82.8	82.8
	slight	125	15.6	15.6	98.4
	medium	12	1.5	1.5	99.9
	severe	1	.1	.1	100.0
	Total	800	100.0	100.0	

Supplementary Table 4E. The frequencies of patients with fear.

		Frequency	Percent	Valid percent	Cumulative percent
Valid	none	747	93.4	93.4	93.4
	slight	46	5.8	5.8	99.1
	medium	7	.9	.9	100.0
	Total	800	100.0	100.0	

Supplementary Table 4F. The frequencies of patients with amnesia.

		Frequency	Percent	Valid percent	Cumulative percent
Valid	none	323	40.4	40.4	40.4
	slight	398	49.8	49.8	90.2
	medium	78	9.8	9.8	100.0
	Total	799	99.9	100.0	
Missing	System	1	.1		
Total		800	100.0		

Supplementary Table 5A. The analysis of cross-classification of palpitation and annoyed mentality in patients with hypertension.

		Annoy			Total
		None	**Slight**	**Medium**	
Palpitation	none	287	104	0	391
	slight	138	219	14	371
	medium	12	14	11	37
	severe	0	1	0	1
Total		437	338	25	800

Supplementary Table 5B. Chi-square tests for analysis of cross-classification of palpitation and annoyed mentality in patients with hypertension.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	194.656[a]	6	.000
Likelihood Ratio	154.725	6	.000
Linear-by-Linear Association	126.564	1	.000
N of Valid Cases	800		

[a]4 cells (33.3%) have expected count less than 5. The minimum expected count is .03.

Supplementary Table 5C. The analysis of cross-classification by palpitation * amnesia crosstabulation.

		Amnesia			Total
		None	**Slight**	**Medium**	
Palpitation	none	192	172	26	390
	slight	124	210	37	371
	medium	7	15	15	37
	severe	0	1	0	1
Total		323	398	78	799

Supplementary Table 5D. Chi-square tests for palpitation * amnesia crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	63.596[a]	6	.000
Likelihood Ratio	49.347	6	.000
Linear-by-Linear Association	38.971	1	.000
N of Valid Cases	799		

[a]4 cells (33.3%) have expected count less than 5. The minimum expected count is .10.

Supplementary Table 6A. The frequencies of patients with backache.

		Frequency	Percent	Valid percent	Cumulative percent
Valid	none	432	54.0	54.0	54.0
	slight	332	41.5	41.5	95.5
	medium	36	4.5	4.5	100.0
	Total	800	100.0	100.0	

Supplementary Table 6B. The frequencies of patients with lumbar debility.

		Frequency	Percent	Valid percent	Cumulative percent
Valid	none	342	42.8	42.8	42.8
	slight	393	49.1	49.1	91.9
	medium	65	8.1	8.1	100.0
	Total	800	100.0	100.0	

Supplementary Table 6C. The frequencies of patients with numbness of limbs.

		Frequency	Percent	Valid percent	Cumulative percent
Valid	none	432	54.0	54.0	54.0
	slight	329	41.1	41.1	95.1
	medium	36	4.5	4.5	99.6
	severe	3	.4	.4	100.0
	Total	800	100.0	100.0	

Supplementary Table 7A. The analysis of cross-classification by palpitation * backache crosstabulation in patients with hypertension.

		Backache			Total
		None	Slight	Medium	
Palpitation	none	279	107	5	391
	slight	135	211	25	371
	medium	18	13	6	37
	severe	0	1	0	1
Total		432	332	36	800

Supplementary Table 7B. Chi-square tests for palpitation * backache crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	109.472[a]	6	.000
Likelihood Ratio	109.468	6	.000
Linear-by-Linear Association	81.646	1	.000
N of Valid Cases	800		

[a]4 cells (33.3%) have expected count less than 5. The minimum expected count is .05.

Supplementary Table 7C. The analysis of cross-classification by palpitation * lumbar debility crosstabulation in patients with hypertension.

		Lumbar debility			Total
		None	Slight	Medium	
Palpitation	none	220	167	4	391
	slight	108	212	51	371
	medium	14	13	10	37
	severe	0	1	0	1
Total		342	393	65	800

Supplementary Table 7D. Chi-square tests for palpitation * lumbar debility crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	98.674[a]	6	.000
Likelihood Ratio	105.634	6	.000
Linear-by-Linear Association	75.273	1	.000
N of Valid Cases	800		

[a]4 cells (33.3%) have expected count less than 5. The minimum expected count is .08.

Supplementary Table 7E. The analysis of cross-classification by palpitation * numbness of limbs crosstabulation in patients with hypertension.

		Numbness of limbs				Total
		None	Slight	Medium	Severe	
Palpitation	none	267	117	7	0	391
	slight	161	191	17	2	371
	medium	4	20	12	1	37
	severe	0	1	0	0	1
Total		432	329	36	3	800

Supplementary Table 7F. Chi-square tests for palpitation * numbness of limbs crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	137.443[a]	9	.000
Likelihood Ratio	106.711	9	.000
Linear-by-Linear Association	96.307	1	.000
N of Valid Cases	800		

[a]8 cells (50.0%) have expected count less than 5. The minimum expected count is .00.

Supplementary Table 8A. The frequencies of patients with dizzy.

		Frequency	Percent	Valid percent	Cumulative percent
Valid	None	315	39.4	39.4	39.4
	slight	447	55.9	55.9	95.3
	medium	38	4.8	4.8	100.0
	Total	800	100.0	100.0	

Supplementary Table 8B. The frequencies of patients being dazed.

		Frequency	Percent	Valid percent	Cumulative percent
Valid	None	409	51.1	51.1	51.1
	Slight	352	44.0	44.0	95.1
	Medium	39	4.9	4.9	100.0
	Total	800	100.0	100.0	

Supplementary Table 8C. The frequencies of patients with headache.

		Frequency	Percent	Valid percent	Cumulative percent
Valid	none	409	51.1	51.1	51.1
	slight	357	44.6	44.6	95.8
	medium	33	4.1	4.1	99.9
	severe	1	.1	.1	100.0
	Total	800	100.0	100.0	

Supplementary Table 8D. The frequencies of patients with tinnitus.

		Frequency	Percent	Valid percent	Cumulative percent
Valid	None	331	41.4	41.4	41.4
	Slight	442	55.3	55.3	96.6
	Medium	27	3.4	3.4	100.0
	Total	800	100.0	100.0	

Supplementary Table 9A. The analysis of cross-classification by palpitation * dizzy crosstabulation in patients with hypertension.

		Dizzy			Total
		None	Slight	Medium	
Palpitation	none	237	145	9	391
	slight	76	277	18	371
	medium	2	24	11	37
	severe	0	1	0	1
Total		315	447	38	800

Supplementary Table 9B. Chi-square tests for palpitation * dizzy crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	192.276[a]	6	.000
Likelihood Ratio	175.322	6	.000
Linear-by-Linear Association	148.627	1	.000
N of Valid Cases	800		

[a]4 cells (33.3%) have expected count less than 5. The minimum expected count is .05.

Supplementary Table 9C. The analysis of cross-classification by palpitation * dazed crosstabulation in patients with hypertension.

		Dazed			Total
		None	Slight	Medium	
Palpitation	none	254	132	5	391
	slight	139	207	25	371
	medium	16	12	9	37
	severe	0	1	0	1
Total		409	352	39	800

Supplementary Table 9D. Chi-square tests for palpitation * dazed crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	93.803[a]	6	.000
Likelihood Ratio	84.350	6	.000
Linear-by-Linear Association	65.320	1	.000
N of Valid Cases	800		

[a]4 cells (33.3%) have expected count less than 5. The minimum expected count is .05.

Supplementary Table 9E. The analysis of cross-classification by palpitation * headache crosstabulation in patients with hypertension.

		Headache				Total
		None	Slight	Medium	Severe	
Palpitation	none	284	102	5	0	391
	slight	112	236	22	1	371
	medium	13	18	6	0	37
	severe	0	1	0	0	1
Total		409	357	33	1	800

Supplementary Table 9F. Chi-square tests for palpitation * headache crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	155.376[a]	9	.000
Likelihood Ratio	156.455	9	.000
Linear-by-Linear Association	122.742	1	.000
N of Valid Cases	800		

[a]8 cells (50.0%) have expected count less than 5. The minimum expected count is .00.

Supplementary Table 9G. The analysis of cross-classification by palpitation * tinnitus crosstabulation in patients with hypertension.

		Tinnitus			Total
		None	Slight	Medium	
Palpitation	none	211	179	1	391
	slight	108	246	17	371
	medium	12	16	9	37
	severe	0	1	0	1
Total		331	442	27	800

Supplementary Table 9H. Chi-square tests for palpitation * tinnitus crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	106.500[a]	6	.000
Likelihood Ratio	86.896	6	.000
Linear-by-Linear Association	63.782	1	.000
N of Valid Cases	800		

[a]4 cells (33.3%) have expected count less than 5. The minimum expected count is .03.

Supplementary Table 10. Descriptive statistics of blood routine index.

	N	Minimum	Maximum	Mean	Std. deviation
Homocysteine (μM)	800	.65	72.80	12.7811	7.39702
Triglyceride (mM)	800	.00	36.00	2.0748	2.03663
Total cholesterol (mM)	800	.42	30.93	4.68563	1.906583
Low density lipoprotein (mM)	799	.98	6.55	2.9852	.83837
High density lipoprotein (mM)	800	.52	11.68	1.8905	1.52829
Fasting blood glucose (mM)	799	2.68	70.19	6.4389	4.51333
Creatinine (μM)	800	30.0	694.2	74.423	40.0658
Urea nitrogen (mM)	800	2.16	469.00	43.0038	102.07597
Uric acid (μM)	800	3.5	766.3	290.880	137.5726
High sensitivity C reactive protein (mg/L)	799	.2	17.3	2.953	2.9505
Valid N (listwise)	797				

Supplementary Table 11A. Correlations of grade of palpitation and homocysteine value in patients with hypertension.

			Palpitation	Homocysteine
Spearman's rho	**Palpitation**	Correlation Coefficient	1.000	.257**
		Sig. (2-tailed)	.	.000
		N	800	800
	Homocysteine	Correlation Coefficient	.257**	1.000
		Sig. (2-tailed)	.000	.
		N	800	800

**Correlation is significant at the 0.01 level (2-tailed).

Supplementary Table 11B. Correlations of grade of palpitation and total cholesterol value in patients with hypertension correlations.

			Palpitation	Total cholesterol
Spearman's rho	**Palpitation**	Correlation Coefficient	1.000	.178**
		Sig. (2-tailed)	.	.000
		N	800	800
	Total cholesterol	Correlation Coefficient	.178**	1.000
		Sig. (2-tailed)	.000	.
		N	800	800

**Correlation is significant at the 0.01 level (2-tailed).

Supplementary Table 11C. Correlations of grade of palpitation and creatinine value in patients with hypertension correlations.

			Palpitation	Creatinine
Spearman's rho	**Palpitation**	Correlation Coefficient	1.000	.087*
		Sig. (2-tailed)	.	.014
		N	800	800
	Creatinine	Correlation Coefficient	.087*	1.000
		Sig. (2-tailed)	.014	.
		N	800	800

*Correlation is significant at the 0.05 level (2-tailed).

Supplementary Table 11D. Correlations of grade of palpitation and uric acid value in patients with hypertension correlations.

			Palpitation	Uric acid
Spearman's rho	**Palpitation**	Correlation Coefficient	1.000	.203**
		Sig. (2-tailed)	.	.000
		N	800	800
	Uric acid	Correlation Coefficient	.203**	1.000
		Sig. (2-tailed)	.000	.
		N	800	800

**Correlation is significant at the 0.01 level (2-tailed).

Supplementary Table 11E. Correlations of grade of palpitation and triglyceride value in patients with hypertension correlations.

			Palpitation	Triglyceride
Spearman's rho	**Palpitation**	Correlation Coefficient	1.000	-.224**
		Sig. (2-tailed)	.	.000
		N	800	800
	Triglyceride	Correlation Coefficient	-.224**	1.000
		Sig. (2-tailed)	.000	.
		N	800	800

**Correlation is significant at the 0.01 level (2-tailed).

Supplementary Table 11F. Correlations of grade of palpitation and high-density lipoprotein value in patients with hypertension Correlations.

			Palpitation	High density lipoprotein
Spearman's rho	**Palpitation**	Correlation Coefficient	1.000	-.156**
		Sig. (2-tailed)	.	.000
		N	800	800
	High density lipoprotein	Correlation Coefficient	-.156**	1.000
		Sig. (2-tailed)	.000	.
		N	800	800

**Correlation is significant at the 0.01 level (2-tailed).

Supplementary Table 12. Gender.

		Frequency	Percent	Valid percent	Cumulative percent
Valid	Male	310	38.8	38.8	38.8
	Female	490	61.3	61.3	100.0
	Total	800	100.0	100.0	

Supplementary Table 13. Family medical history.

		Frequency	Percent	Valid percent	Cumulative percent
Valid	No	628	78.5	78.7	78.7
	Yes	170	21.3	21.3	100.0
	Total	798	99.8	100.0	
Missing	System	2	.3		
Total		800	100.0		

Supplementary Table 14A. The analysis of cross-classification by palpitation * Age crosstabulation in patients with hypertension.

		Palpitation				Total
		None	Slight	Medium	Severe	
Age Grades	40-49	10	6	0	0	16
	50-59	5	0	0	0	5
	60-69	165	135	6	0	306
	>69	211	230	31	1	473
Total		391	371	37	1	800

Supplementary Table 14B. Chi-square tests for palpitation * age crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	20.245[a]	9	.016
Likelihood Ratio	24.106	9	.004
Linear-by-Linear Association	14.290	1	.000
N of Valid Cases	800		

[a]8 cells (50.0%) have expected count less than 5. The minimum expected count is .01.

Supplementary Table 14C. The analysis of cross-classification by angina * age crosstabulation in patients with hypertension.

		Angina			Total
		None	Slight	Medium	
Age Grades	40-49	12	4	0	16
	50-59	4	1	0	5
	60-69	238	63	5	306
	>69	352	119	2	473
Total		606	187	7	800

Supplementary Table 14D. Chi-square tests for angina * age crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	5.296[a]	6	.506
Likelihood Ratio	5.356	6	.499
Linear-by-Linear Association	.317	1	.574
N of Valid Cases	800		

[a]7 cells (58.3%) have expected count less than 5. The minimum expected count is .04.

Supplementary Table 14E. The analysis of cross-classification by amnesia * age crosstabulation in patients with hypertension.

		Amnesia			Total
		None	Slight	Medium	
Age Grades	40-49	5	9	2	16
	50-59	4	1	0	5
	60-69	129	153	24	306
	>69	185	235	52	472
Total		323	398	78	799

Supplementary Table 14F. Chi-square tests for amnesia * age crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	6.228[a]	6	.398
Likelihood Ratio	6.611	6	.358
Linear-by-Linear Association	.868	1	.351
N of Valid Cases	799		

[a]4 cells (33.3%) have expected count less than 5. The minimum expected count is .49.

Supplementary Table 14G. The analysis of cross-classification by annoy * age crosstabulation in patients with hypertension.

		Annoy			Total
		None	Slight	Medium	
Age Grades	40-49	12	3	1	16
	50-59	4	1	0	5
	60-69	167	131	8	306
	>69	254	203	16	473
Total		437	338	25	800

Supplementary Table 14H. Chi-square tests for annoy * age crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	5.642[a]	6	.465
Likelihood Ratio	6.192	6	.402
Linear-by-Linear Association	1.652	1	.199
N of Valid Cases	800		

[a]4 cells (33.3%) have expected count less than 5. The minimum expected count is .16.

Supplementary Table 14I. The analysis of cross-classification by numbness of limbs * age crosstabulation in patients with hypertension.

		Numbness of limbs				Total
		None	Slight	Medium	Severe	
Age Grades	40-49	13	3	0	0	16
	50-59	3	2	0	0	5
	60-69	184	116	6	0	306
	>69	232	208	30	3	473
Total		432	329	36	3	800

Supplementary Table 14J. Chi-square tests for numbness of limbs * age crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	21.136[a]	9	.012
Likelihood Ratio	24.133	9	.004
Linear-by-Linear Association	18.789	1	.000
N of Valid Cases	800		

[a]8 cells (50.0%) have expected count less than 5. The minimum expected count is .02.

Supplementary Table 14K. The analysis of cross-classification by lumbar debility * age crosstabulation in patients with hypertension.

		Debility of lumbar			Total
		None	Slight	Medium	
Age Grades	40-49	5	10	1	16
	50-59	3	2	0	5
	60-69	153	125	28	306
	>69	181	256	36	473
Total		342	393	65	800

Supplementary Table 14L. Chi-square tests for lumbar debility * age crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	15.193[a]	6	.019
Likelihood Ratio	15.634	6	.016
Linear-by-Linear Association	2.429	1	.119
N of Valid Cases	800		

[a]4 cells (33.3%) have expected count less than 5. The minimum expected count is .41.

Supplementary Table 14M. The analysis of cross-classification by backache * age crosstabulation in patients with hypertension.

		Backache			Total
		None	Slight	Medium	
Age Grades	40-49	14	1	1	16
	50-59	1	4	0	5
	60-69	165	122	19	306
	>69	252	205	16	473
Total		432	332	36	800

Supplementary Table 14N. Chi-square tests for backache * age crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	15.233[a]	6	.019
Likelihood Ratio	17.486	6	.008
Linear-by-Linear Association	.449	1	.503
N of Valid Cases	800		

[a]4 cells (33.3%) have expected count less than 5. The minimum expected count is .22.

Supplementary Table 14O. The analysis of cross-classification by dizzy * age crosstabulation in patients with hypertension.

		Dizzy			Total
		None	Slight	Medium	
Age Grades	40-49	9	6	1	16
	50-59	2	3	0	5
	60-69	138	158	10	306
	>69	166	280	27	473
Total		315	447	38	800

Supplementary Table 14P. Chi-square tests for dizzy * age crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	11.447[a]	6	.076
Likelihood Ratio	11.765	6	.067
Linear-by-Linear Association	9.168	1	.002
N of Valid Cases	800		

[a]4 cells (33.3%) have expected count less than 5. The minimum expected count is .24.

Supplementary Table 14Q. The analysis of cross-classification by dazed * age crosstabulation in patients with hypertension.

		Dazed			Total
		None	Slight	Medium	
Age Grades	40-49	13	3	0	16
	50-59	3	2	0	5
	60-69	179	116	11	306
	>69	214	231	28	473
Total		409	352	39	800

Supplementary Table 14R. Chi-square tests for dazed * age crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	19.914[a]	6	.003
Likelihood Ratio	21.204	6	.002
Linear-by-Linear Association	18.901	1	.000
N of Valid Cases	800		

[a]4 cells (33.3%) have expected count less than 5. The minimum expected count is .24.

Supplementary Table 14S. The analysis of cross-classification by headache * age crosstabulation in patients with hypertension.

		Headache				Total
		None	Slight	Medium	Severe	
Age Grades	40-49	12	3	1	0	16
	50-59	5	0	0	0	5
	60-69	169	131	5	1	306
	>69	223	223	27	0	473
Total		409	357	33	1	800

Supplementary Table 14T. Chi-square tests for headache * age crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	21.597[a]	9	.010
Likelihood Ratio	25.329	9	.003
Linear-by-Linear Association	11.744	1	.001
N of Valid Cases	800		

[a]8 cells (50.0%) have expected count less than 5. The minimum expected count is .01.

Supplementary Table 14U. The analysis of cross-classification by Tinnitus * age crosstabulation in patients with hypertension.

		Tinnitus			Total
		None	Slight	Medium	
Age Grades	40-49	14	2	0	16
	50-59	3	2	0	5
	60-69	143	155	8	306
	>69	171	283	19	473
Total		331	442	27	800

Supplementary Table 14V. Chi-square tests for tinnitus * age crosstabulation.

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	24.168[a]	6	.000
Likelihood Ratio	25.325	6	.000
Linear-by-Linear Association	21.611	1	.000
N of Valid Cases	800		

[a]4 cells (33.3%) have expected count less than 5. The minimum expected count is .17.