

# Hypertension and Cerebrovascular Diseases: A Large Long Term Followed Up Cohort Hypertension Patients

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## Research Article

**Keywords:** Cerebrovascular disease, Hypertension, Retrospective cohort, follow up, Stroke

**Posted Date:** January 4th, 2021

**DOI:** <https://doi.org/10.21203/rs.3.rs-135851/v1>

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## Abstract

**Background:** Cerebrovascular disease (CVD) is the first cause of death in Chinese residents [1]. Hypertension (HP) has been shown to be the single most important modifiable risk factor among multiple etiologies. The incidence of stroke has increased gradually and has begun occurring at a younger age in recent years [1-2]. There were few related studies on CVD of HP cohort.

**Objective:** To explore CVD distribution and epidemic characteristics in followed-up hypertension patients.

**Methods:** Using the Hypertension Follow-up Management System database in Jiading district in Shanghai. We designed a retrospective cohort study that included all followed-up hypertension patients between 2002 and 2020. The endpoint was the occurrence of CVD confirmed by the hospital; otherwise, the patients were tracked until September 30, 2020. Record information of every patient has been collected in the registration card and each followed-up record.

**Results:** Among 166688 followed-up HP patients, the total cumulative incidence of CVD was 6.68% (male 7.02%, female 6.37%) during follow-up period, cumulative incidence of ischemic CVD, hemorrhagic CVD and unclassified stroke was respectively 4.76%, 0.40% and 1.53%. Cumulative incidence of CVD increased with age, the group under 30 was 0, and the group over 70 was the highest (9.24%). The higher blood pressure was, the higher prevalence of CVD was. The prevalence of CVD increased with duration of HP, 3.76% within one year and 11.34% after 10 years. The proportion of CVD cases in HP patients from April to June was the largest in the four seasons; the proportion of patients from October to December was the minimum.

**Conclusion:** Hypertension patient was prone to falling cerebrovascular disease; the main type of disease was cerebral infarction. Male incidence was higher than female incidence. The cumulative incidence of CVD increased with age, blood pressure and duration of HP patients. It had seasonal characteristics, which was relatively high from April to June within year.

## Introduction

A recent study showed that the standardized prevalence of stroke among residents aged 40 or above increased from 1.89% (2012) to 2.32% (2018), the incidence rate of residents among 40 ~ 74 years old was increasing with an average annual rate of 8.3% in China [1–2]. The latest reports of GBD (Global Burden of Disease Study) showed China's overall lifetime risk of stroke was 39.9%, ranking the first in the world, which means that about two out of five people would suffer from stroke in their lifetime [3–4]. It's reported that hypertension led 10.4 million deaths worldwide, it was effectively associated with stroke and worse prognosis, and it was the first modifiable vascular risk factor [5]. Most of the incidence of SVD related strokes might cause by raised blood pressure [6]. The burden of cerebrovascular disease increased with the increase of the number of the elderly. Hypertension, diabetes, dyslipidemia, diet, smoking and physical activity played efficient role in stroke related diseases [2, 5, 6].

In order to better observe and explore the regular characteristics between hypertension and cerebrovascular disease, a large long term follow-up cohort of hypertension patients have established in Shanghai China. It was designed to mainly explore regular pattern of the main population of hypertensive patients with cerebrovascular disease, the time of occurrence, the type of lesions and so on. The purpose of this study was to explore the baseline characteristics of cerebrovascular diseases in hypertension, and the association between hypertension and cerebrovascular diseases base on a large long term follow-up cohort hypertension patients.

## Methods

### Data sources

The Hypertension Follow-up Management System was officially built and implemented in Jiading district in Shanghai China in 2002. The patients with hypertension in community were registered, investigated, filed and followed up regularly by community health workers or family doctors. The Hypertension Follow-up Management System Database records the medical information of all registered and followed-up hypertension patients. During this period, 56409 HP patients dropped out of the cohort due to death or emigration or so on, and 168417 patients registered because of diagnosed hypertension. The database includes approximately 166688 patients in Jiading district in Shanghai. All patients entered the observation queue, and the cohort of hypertension patients was dynamic. Dynamic changes of the HP cohort see Fig. 1. All about cerebrovascular disease occurred in patients must be recorded in detail. Cerebrovascular disease must be diagnosed and confirmed by a senior hospital. The study was approved by Science and Technology Commission, Health Commission and CDC in Jiading district in Shanghai. All methods were carried out in accordance with relevant guidelines and regulations.

## Study Objects And Data Collection

All study objects were from the above Hypertension Follow-up Management System, and observation deadline of data of study objects were collected was September 30, 2020. Clinical information and biological information for each hypertension patient in the registration card and each followed-up record were collected. Their socio-demographic status (birth date, gender, habitation, occupation and education level), etiology of family history, disease history (disease kind, diagnosed date and diagnosed hospital), lifestyle (smoking, drinking and exercise) and blood pressure and so on were documented. Objects of hypertension patients in this study were primary hypertension, excluding secondary hypertension patients. Cerebrovascular disease refers to that the onset date was later than the date of hypertension diagnosed and registration, Cases were excluded if onset date was before or close (within one month) the date of hypertension diagnosed and registration.

## Definition And Classification

According to the classification of diseases and ICD-10 coding rules, and to facilitate this statistical analysis, cerebrovascular diseases mainly included ischemic cerebrovascular diseases, hemorrhagic cerebrovascular diseases and unclassified stroke (I64) in this study. Ischemic cerebrovascular diseases include transient ischemic attack (G65), cerebral infarction (I63). Hemorrhagic cerebrovascular diseases included subarachnoid hemorrhage (I60), intracerebral hemorrhage (I61) and other non-traumatic intracranial hemorrhage (I62).

Observation starting point: refers to the time point when hypertension patients were registered and entered the follow-up management queue.

Observation end point: refers to the time when hypertension patients have expected outcome events (stroke) or withdraw from the observation queue due to loss of follow-up. Follow up time or observation duration: refers to the time difference between the end point and the starting point (observation end point minus observation starting point).

## Statistical analysis

All databases in the Hypertension Follow-up Management System were exported into Microsoft Excel database according to the cut-off time prescribed above, and then the relevant logical examination, data screening and conversion were carried out. Statistical analyses were performed using the statistical software package (IBM SPSS statistics version 21). Mean and standard deviation (SD) were used to compute for quantitative variables, and comparisons between groups were performed by t-test. Number (n) and percentage (%) were computed for the categorical data, comparisons between groups were performed by the chi-square ( $\chi^2$ ) test. All results were statistically significant if the two tailed p value was less than 0.05.

## Results

### Baseline demographic and clinical characteristics

A total of 166 688 studied hypertension patients (80251 male, 86437 female; mean age:  $63.16 \pm 11.22$  years old) were included in this final data analysis. Among these hypertension patients, the blood pressure value at the time of registry: systolic blood pressure was  $154.49 \pm 13.83$  mmHg; diastolic blood pressure was  $92.57 \pm 8.74$  mmHg. Overall, 11143 hypertension patients had developed cerebrovascular diseases (CVD) from hypertension before the deadline, and cumulative incidence of CVD was 6.68%. The mean age of hypertension patients complicated by cerebrovascular disease was  $73.44 \pm 10.39$  years old and the average observation duration or followed up time was  $5.83 \pm 3.95$  years.

Figure 2 showed that the types and incidence of 11143 cerebrovascular disease in hypertension patients, 7932 cases were ischemic cerebrovascular (the proportion was 71.18% and cumulative incidence was 4.76%); 663 cases were hemorrhagic cerebrovascular (the proportion was 5.95% and cumulative incidence was 0.40%); 2548 cases were unclassified stroke (the proportion was 22.87% and cumulative incidence was 1.53%). In the ischemic cerebrovascular, there were 7609 (cumulative incidence was 4.56%) cerebral infarction (CIS, I63), 323 (cumulative incidence was 0.19%) transient ischemic attack (TIA, G65). In the hemorrhagic cerebrovascular, there were 133 (cumulative incidence was 0.08%) subarachnoid hemorrhage (SAH, I60), 491 (cumulative incidence was 0.29%) intracerebral hemorrhage (ICH, I61), 39 (cumulative incidence was 0.02%) non-traumatic intracranial hemorrhage (NTICH, I62).

### Hp Characteristics And Cvd

In this followed up observational cohort of hypertension patients, the cerebrovascular disease (CVD) cumulative incidence of male was 7.02% (5636/80251), and female was 6.37% (5507/86437). Male was higher than female ( $\chi^2 = 35.385$ ,  $p < 0.001$ ). Age distribution: the CVD cumulative incidence in HP patients under 30 years old were 0% (0/40), 30 ~ 39 years old 2.01% (21/1047), 40 ~ 49 years old 2.39% (135/5641), 50 ~ 59 years old 4.20% (911/21671), 60 ~ 69 years old 4.44% (2492/56186), over 70 years old 9.24% (7584/82103). There was no CVD case in the hypertension patients group under 30 years old and cumulative incidence of CVD was the highest in the age group over 70 years old. Cumulative incidence of CVD increased with age ( $\chi^2 = 82.174$ ,  $p < 0.001$ ). See Table 1.

Table 1

Cumulative incidence of cerebrovascular diseases in hypertensive patients with different sex, age and blood pressure type (n, %)

		N	Unclassified stroke(164) n (%)	Ischemic cerebrovascular			Hemorrhagic cerebrovascular			Total n (%)	$\chi^2$ p	
				CIS (163)	TIA (G45)	Total n (%)	SAH (160)	ICH (161)	NTICH (162)			Total n (%)
Sex	male	80251	1373 (1.71%)	3754	158	3912 (4.87%)	66	268	17	351 (0.44%)	5636 (7.02%)	$\chi^2 =$ 35.385
	Female	86437	1175 (1.36%)	3855	165	4020 (4.65%)	67	223	22	312 (0.36%)	5507 (6.37%)	p < 0.001
Age (y)	< 30	40	0 (0.00%)	0	0	0 (0.00%)	0	0	0	0 (0.00%)	0 (0.00%)	$\chi^2 =$ 82.174
	30~	1047	2 (0.19%)	15	1	16 (1.53%)	0	3	0	3 (0.29%)	21 (2.01%)	p < 0.001
	40~	5641	13 (0.23%)	110	3	113 (2.00%)	1	8	0	9 (0.16%)	135 (2.39%)	
	50~	21671	66 (0.30%)	755	40	795 (3.67%)	6	42	2	50 (0.23%)	911 (4.20%)	
	60~	56186	141 (0.25%)	2104	91	2195 (3.91%)	28	114	14	156 (0.28%)	2492 (4.44%)	
	≥ 70	82103	2326 (2.83%)	4625	188	4813 (5.86%)	98	324	23	445 (0.54%)	7584 (9.24%)	
BP	High SBP	31747	428 (1.35%)	1474	51	1525 (4.80%)	31	100	7	138 (0.43%)	2091 (6.59%)	$\chi^2 =$ 23.883
	High DBP	4553	64 (1.41%)	859	44	903 (19.83%)	14	66	3	83 (1.82%)	1050 (23.06%)	p < 0.001
	HBP	130388	2057 (1.58%)	5275	228	5503 (4.22%)	88	325	29	442 (0.34%)	8002 (6.14%)	
Total		166688	2548 (1.53%)	7609 (4.56%)	323 (0.19%)	7932 (4.76%)	133 (0.08%)	491 (0.29%)	39 (0.02%)	663 (0.40%)	11143 (6.68%)	

(Note: TIA = transient ischemic attack; CIS = cerebral ischemic stroke /Cerebral infarction; TIA: transient ischemic attack; SAH = subarachnoid hemorrhage; ICH: intracerebral hemorrhage; NTICH: non-traumatic intracranial hemorrhage; n(%) = number (cumulative incidence %); High SBP = only high systolic blood pressure; High DBP = only high diastolic blood pressure; HBP = high systolic and diastolic blood pressure)

Among these cerebrovascular disease in hypertension patients, the proportion of ischemic cerebrovascular, hemorrhagic cerebrovascular and unclassified stroke were respectively 71.17%, 5.95% and 22.88% of the total number of CVD. Cerebral infarction (CIS) and transient ischemic attack (TIA) were respectively 68.28% and 2.90% of the total number of CVD in ischemic CVD; subarachnoid hemorrhage (SAH), intracerebral hemorrhage (ICH) and non-traumatic intracranial hemorrhage (NTICH) were respectively 1.19%, 4.41% and 0.35% of the total number of CVD. The observation results of this hypertension cohort showed that ischemic CVD was the most important type of CVD in HP patients.

Figure 3 showed cumulative incidence of CVD was different in different levels of registered blood pressure of HP patients ( $\chi^2 = 113.895$ ,  $p < 0.001$ ). When  $140\text{mmHg} \leq \text{SBP} < 160 \text{mmHg}$  or  $90\text{mmHg} \leq \text{DBP} < 100 \text{mmHg}$  (Called grad I), cumulative incidence of CVD was 6.34% (6074/89744);  $160\text{mmHg} \leq \text{SBP} < 180 \text{mmHg}$  or  $100\text{mmHg} \leq \text{DBP} < 110 \text{mmHg}$  (Called grad II), cumulative incidence of CVD was 6.69% (3521/ 49137);  $180\text{mmHg} \leq \text{SBP}$  or  $110\text{mmHg} \leq \text{DBP}$  (Called grad III), cumulative incidence of CVD was 8.50% (1548/16664). The higher the registered blood pressure was, the higher the cumulative incidence of CVD was. Table 1 showed that cumulative incidence of CVD was different in different types of hypertension, cumulative incidence of CVD was 6.59% (2091/31747) in high SBP (only high systolic blood pressure) patients; 23.06% (1050/4553) in high DBP (only high diastolic blood pressure); 6.14% (8002/130388) in HBP (systolic and diastolic blood pressure were high). The results showed that cumulative incidence of CVD in high DBP was significantly higher than that in other patients ( $\chi^2 = 23.883$ ,  $p < 0.001$ ).

## Hp Duration And Cvd

With the extension of the duration of hypertension, cumulative incidence of CVD will continue to increasing, cumulative incidence of CVD was 3.76% within one year and 11.34% after 10 years. Cumulative incidence of different types of cerebrovascular diseases was also different ( $\chi^2 = 173.546$ ,  $p < 0.001$ ). See Fig. 4. Generally speaking, the peak of cumulative incidence of CVD in hypertension patients was 9–10 years after the registered and followed-up. After that, cumulative incidence will drop slightly, and the clam will remain at a high level. Cumulative incidence of

ischemic CVD would continue to increasing with the extension of the duration of hypertension. Cumulative incidence of hemorrhage CVD had been maintained at a low level, and the fluctuation range was not very large. In fact, unclassified stroke also included cerebral infarction and hemorrhage cerebrovascular disease; therefore, the changed trend of its incidence rate was basically consistent with that of the overall cerebrovascular disease.

## Seasons Distribution Of Cvd

Among 11143 CVD in HP patients, season distribution was different. From January to December, the proportion of CVD in HP patients were respectively 7.53% 7.29% 8.55% 8.96% 9.71% 9.10% 9.63% 8.13% 8.01% 8.15% 7.19% and 7.76%, The difference of the proportion of different types of CVD in different months was obvious ( $\chi^2 = 149.439$ ,  $p < 0.001$ ). The proportion of patients from January to March accounted for 23.51% of the total number of patients; that from April to June accounted for 27.03%; from July to September accounted for 26.13%; and from October to December accounted for 23.32%. The difference of the proportion of different types of CVD in different seasons was obvious ( $\chi^2 = 60.656$ ,  $p < 0.001$ ). See Fig. 5. Comparatively speaking, the number of patients of CVD from April to June was the largest in the four seasons; the next was that from July to September; the number of patients from October to December was the minimum.

## Discussion

In this study, Among 166688 followed-up hypertension patients, the total cumulative incidence of CVD was 6.68% during followed-up period, the male patient was 7.02%, and the female patient was 6.37%. And cumulative incidence of ischemic CVD, hemorrhagic CVD and unclassified stroke were respectively 4.76%, 0.40% and 1.53%. Ischemic CVD was the most important type of cerebrovascular disease in hypertension patients in Jiading Shanghai China. Cumulative incidence of CVD in hypertension patients with was significantly higher than that of non-hypertensive patients people reported in the past in China [1, 2, 7]. The result of this long-term followed-up for hypertension showed that cumulative incidence of CVD in hypertension patients was significantly higher than that in normal population. Stroke was the first cause of death in China and the second cause of death in the world [8]. Primary prevention was particularly important because about 77% of strokes were first events [9]. Specifically, hypertension was a well-recognized major risk factor for stroke [10–11]. The kind of effective strategy for preventing stroke was controlling the risk factors of stroke [12]. Risk of stroke increased in patients with hypertensive pregnancy disorders, compared with those without disorder; the patients who had experienced the disorders had a 2.134 fold higher risk of developing stroke in the future [13]. Hypertension can cause cerebral infarction, which was the most important factor of cerebral infarction. Because long-term high blood pressure can lead to cerebral vasospasm, resulting in blood stasis, the formation of embolism [14].

The results of long-term followed-up of HP patients showed that cumulative incidence of CVD increased with age, blood pressure and duration of HP patients. The CVD cumulative incidence of patients under 30 years old were 0%, 30 ~ 39 years old 2.01%, 40 ~ 49 years old 2.39%, 50 ~ 59 years old 4.20%, 60 ~ 69 years old 4.44%, over 70 years old 9.24%. There was no CVD case in the hypertension patients group under 30 years old and cumulative incidence of CVD was the highest in the age group over 70 years old. The older the age was, the higher the cumulative incidence was. Cumulative incidence of CVD of grad I, grad II and grad III blood pressure were respectively 6.34%, 6.69% and 8.50%. Cumulative incidence of CVD was different in different types of HP patients; cumulative incidence was 6.59% in only high systolic blood pressure patients; 23.06% in only high diastolic blood pressure patients; 6.14% in high systolic and diastolic blood pressure patients. The results remind us that the risk of high diastolic blood pressure was higher than that of systolic blood pressure. Some studies showed that hypertension was the most important risk factor for stroke [10, 15–17]; Hypertensive patients with > 80 bpm had the highest risk of stroke [18]. In addition, this study result showed that hypertension duration was associated with the increased prevalence of CVD, the prevalence of ischemic CVD would continue to increasing with the extension of the duration of hypertension. These research results reminded us that CVD was related to the control of blood pressure level, age, diet and drugs of patients with hypertension [19–21].

The result in this study showed that season distribution of CVD in HP patients was different, CVD incidence varied from month to month. In terms of months, the cumulative incidence was relatively high from May to July. In terms of seasons, the number of patients from January to March accounted for 23.51% of the total number of patients; that from April to June accounted for 27.03%; from July to September accounted for 26.13%; and from October to December accounted for 23.32%. Comparatively speaking, the number of patients of CVD from April to June was the largest in the four seasons; the next was that from July to September; the number of patients from October to December was the minimum. It reminds us that we should pay attention to the seasonal changes in the prevention and control of hypertension in the community.

A recent study revealed that although patients were more likely to survive after stroke, poorer recovery was noted [22]. The disease of CVD, not only seriously endangers Chinese residents, but also has a serious impact on other countries or region area in the world [23–25]. Some studies told us many patients are exposed to a lot of risk factors (especially sub-health status plus bad lifestyle and living habits), but these patients did not know they were facing the risk of stroke [26–29]. Therefore, we should pay attention to the prevention and control of CVD, the prevention and control of cerebrovascular disease in patients with hypertension, especially to strengthen the prevention and control of cerebral infarction in patients with hypertension.

## Abbreviations

### HP

hypertension; **BP**:blood pressure; **SBP**:systolic blood pressure; **DBP**:diastolic blood pressure; **ICD**:international classification of diseases; **CVD**:cerebrovascular diseases; **ICVD**:Ischemic cerebral vascular disease; **SAH**:subarachnoid hemorrhage; **ICH**:intracerebral hemorrhage; **CIS**:cerebral ischemic stroke /cerebral infarction; **TIA**:transient ischemic attack; **NTICH**:non-traumatic intracranial hemorrhage. **CI**:Cumulative incidence

## Declarations

### Acknowledgements

Not applicable

### Authors' contributions

All authors have read and approved the manuscript. An-le LI: substantial contributions to the conception and design of the study, analysis of the data, interpretation of data and the drafting and revision of the paper. Shuai Zhu: substantial contributions to the data acquisition, merging and sorting. Zhi-hao Hu, Qian Peng, Xiang Fang, Yi-ying Zhang: substantial contributions to the data acquisition and data quality control. Final approval of manuscript: All authors.

### Funding

This study was funded by Research project of Natural Science Foundation of Jiading district in Shanghai (JDKW-2020-0036). The funder played no role in the design; conception; data collection, interpretation, and analysis; drafting; or any other process in this paper.

### Availability of data and materials

The data that support the findings of this study are available from the Hypertension Follow-up Management System database in Jiading district in Shanghai, but restrictions apply regarding the availability of these data, which were used under license for the current study and thus are not publicly available. The data are, however, available from the authors upon reasonable request and with permission of the Jiading district health committee in Shanghai.

### Ethics approval and consent to participate

Ethical approval was granted by Jiading district center for disease control and prevention research ethics committee. All subjects gave informed consent to participate in the study, they would like to participate in registry and manage and answer all the related questions in the follow-up.

### Consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

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## Figures

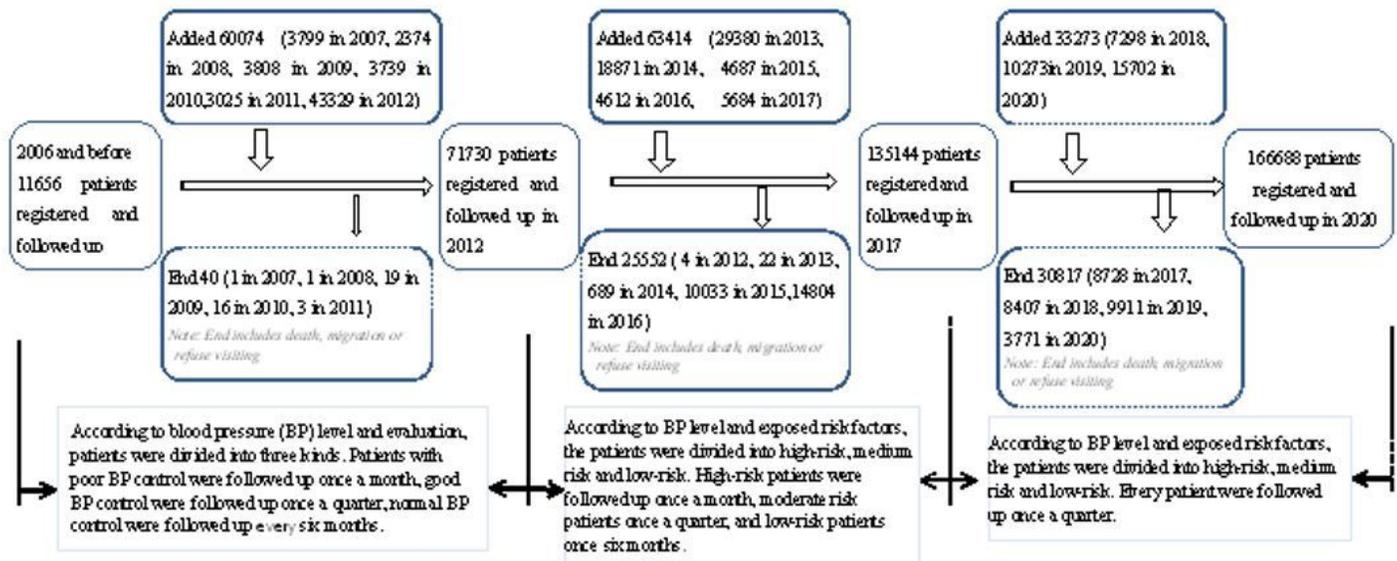


Figure 1

Dynamic changes of follow-up management cohort of hypertension in Jiading Shanghai

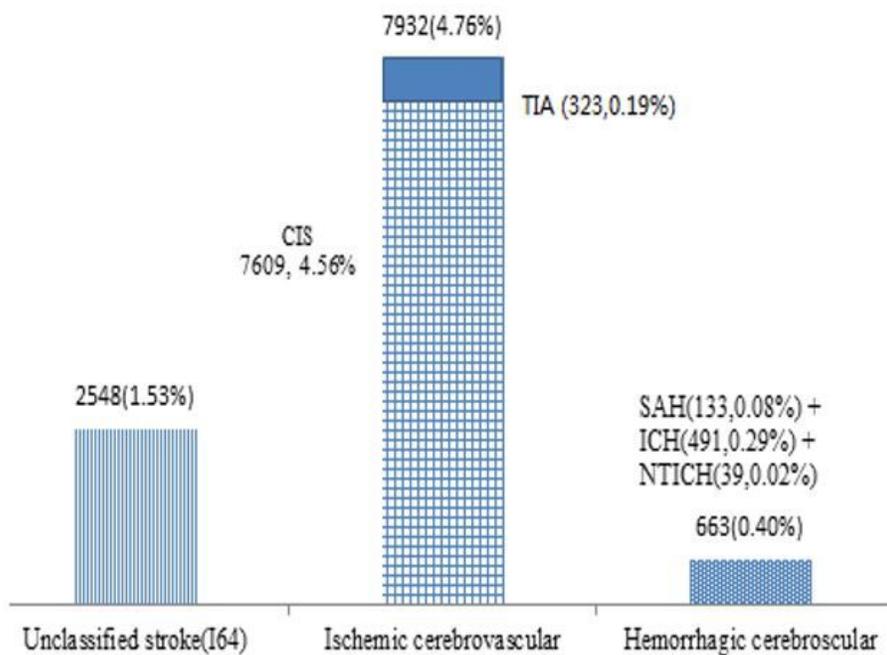


Figure 2

Types and incidence rate of CVD in hypertension patients

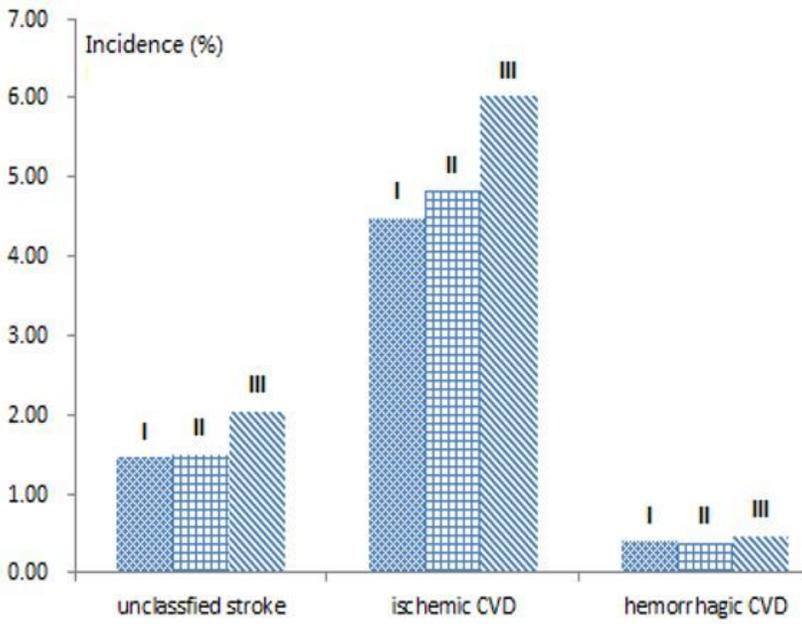


Figure 3

Incidence rate of CVD in different blood pressure grad

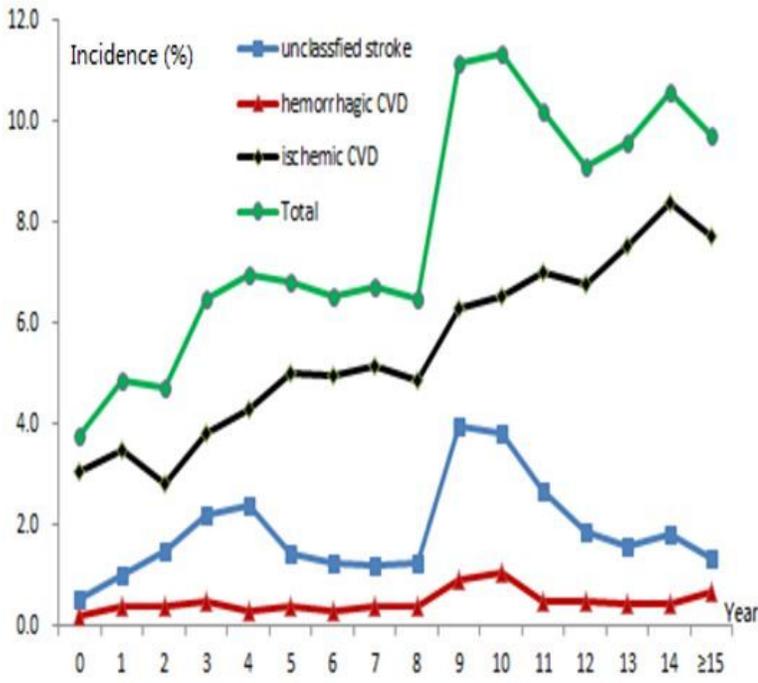
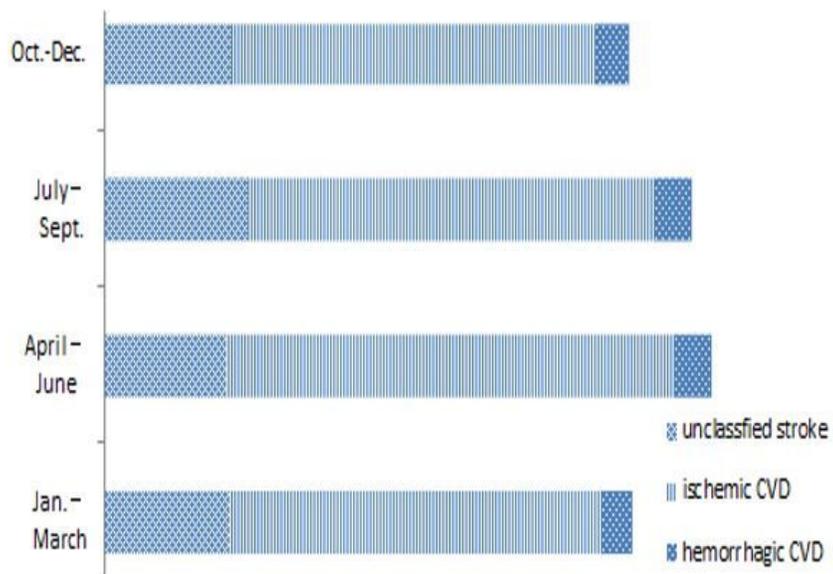


Figure 4

The duration of hypertension and incidence rate of CVD



**Figure 5**

Distribution of CVD in HP patients in different seasons