Characteristics of Masked Hypertension in Diabetes Mellitus Patientstype 2

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Authors' contributions

This work was carried out in collaboration among all authors. Author VTB designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors NLT and LMH managed the analyses of the study. All authors read and approved the final manuscript.

Original Research Article

ABSTRACT

Monitoring blood pressure with a continuous blood pressure monitor to carry around to detect masked hypertension (MH) in type 2 diabetes patients who are on outpatient treatment at Thai Binh Medical University Hospital, Thai Binh, Vietnam.

Objective: Analysis of MH characteristics in type 2 diabetic patients.

Research Methods: Cross-sectional descriptive study, sample size of 186 patients with type 2 diabetes with MH determined by blood pressure monitor 24 hours. Analysis of 24-hour blood pressure results in MH patients.

Results: 186 patients with hypertension / type 2 diabetes, including 77 men and 109 more, the average age is 62.2 ± 9.3 years old, there are 98.9% of hypertensive patients with grade I, only 1.1% of hypertensive patients degree II; MH at night accounted for the highest rate of 43.0%, of which the average systolic blood pressure was 123.8 ± 9.8 mmHg, and diastolic blood pressure was 75.2 ± 6.1 mmHg; On average, the highest increase is around 9 am and 19 pm, slightly down around 13pm and down at the deepest around 2-3am. There is a synchronous variation between systolic and diastolic blood pressure.

Conclusion: Blood pressure should be monitored continuously for 24 hours in all patients with type 2 diabetes to detect and promptly treat MH.

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1. INTRODUCTION

Masked Hypertension (MH) is a condition in which blood pressure is of normal value when measured in the clinic, but increases when measured at home. Recent studies show that MH causes damage to target organs: left ventricular thickening, diastolic dysfunction, carotid artery endothelium thickening, proteinuria and is one of the cardiovascular risk factors compared with patients with truly normal blood pressure [1]. The rate of MH in the general population is about 9-30.9%. Masked hypertension is common in patients with type 2 diabetes and rapidly increases the complications of diabetes as well as damage to the hypertensive target organs (Mendeng et al, 2017). It is necessary to detect MH and characterize variability during 24 hours to be able to control blood pressure, thereby preventing complications in patients with type 2 diabetes.

1.1 Consumption

Survey of MH characteristics with ABPM-Ambulatory Blood Pressure Monitoring in type 2 diabetes patients.

2. METHODOLOGY

2.1 Subjects and Methods of Research

2.1.1 Research design

This is descriptive study with a cross-sectional investigation. Type 2 diabetic patients with normal blood pressure in the clinic, blood pressure is measured with a blood pressure monitor continuously carried to find the patients with MH. Then, blood pressure characteristics were analyzed in these patients.

2.1.2 Research subjects

Patients diagnosed with type 2 diabetes are being treated at Thai Binh Medical University Hospital. Are type 2 diabetic patients with MH.

2.1.3 Selection criteria

-   Patient is being treated or diagnosed with type 2 diabetes for the first time according to the diagnostic standards of the American Diabete Association 2010 (ADA-American Diabete Asscociation).
-   Patient is not taking medicine that affect blood pressure in the last 3 months, (patient who has not been on medication that affects blood pressure for at least 3 months, has a blood pressure of less than 140/90 mmHg when measured in the clinic at the time of visit) with blood pressure measured at the clinic <140/90 mmHg.
-   Do not suffer from other acute diseases which affect blood pressure (acute renal diseases, acute infection, glaucoma…).
-   No serious complications: pre-coma - diabetic coma.
-   Voluntary participation in research.

2.1.4 Exclusion criteria

-   Patients not subject to selection criteria.
-   Patient was diagnosed with hypertension before or at the time of examination (blood pressure measured in the clinic ≥ 140/90 mmHg).
-   The time of continuous blood pressure measurement is < 85% or > 15% of the measuring results do not meet the standards according to the analysis requirements.
-   Suffer from other acute diseases which affect blood pressure (acute renal diseases, acute infection, glaucoma…).
-   Do not agree to take part in research .

2.1.5 Location and time of study

-   Location: Department of Internal Medicine at Thai Binh Medical University Hospital.
-   Time: from January to October 2020.

2.1.6 Sample size and sample selection

Sample size: Calculated according to the formula of the descriptive study. With confidence coefficient calculated as α = 0.05 and 95% confidence interval, relative error of 0.1, the calculated sample size is 181 patients. In our study, there are 186 patients eligible for selection.

Sample selection: convenient accumulation until enough sample is studied.

Research steps:

-   Clinical examination and indication for subclinical exploration of patients.

- Selecting research subjects based on clinical and subclinical examination results: patients with sufficient selection factors and no exclusion factors according to set criteria will be selected to participate in the study.
- Explanation of disease condition, prescribing treatment.
- Counseling, consulting and guiding patients to write a commitment to agree to participate in the study.
- Get a 24-hour blood pressure monitor and guide on any issues related to this probe.
- Appoint the patient to disassemble the device and receive the results after 24 hours from the time the device is installed. Methods of information collection:
- Interview and physical examination of the patient to collect information about the research subjects' history, medical history and clinical symptoms.
- The patient has blood pressure measured at the clinic to determine if there is increased blood pressure.
- Patients who do not have hypertension at the clinic wear 24 hour automatic blood pressure monitor (ABPM) brand Microlife 24h WatchBP 03 of Microlife - Switzerland. Set automatic measurement mode 30 minutes / time during the day (from 7:00 - before 17:00 o'clock), 60 minutes / time at night (from 17:00 the day before to before 7:00 day the next day).

Standards used in research:

- Diagnostic criteria masked hypertension according to the Guidelines of the European Society of Cardiology 2018 [2].
- Divising hypertension stage according to the 7th American Interstate Committee, 2004 [3].
- BMI classification based on recommendations of the World Health Organization recommended for the Asia - Pacific [4].
- The average values of blood pressure are automatically calculated by the programmed formula, in which:

  + Average daytime blood pressure: is the average value of blood pressure from 7:00 am - before 17:00 pm
  + Average night blood pressure: is the average value of blood pressure from after

17:00 pm of the previous day - before 7:00 am of the next day.

2.1.7 Analyzing data

The data entry process was done 2 times by 2 independent people using WHO SPSS 20.0 software. Then cross-check between the two data sets to detect errors.

- Indicators are presented as mean and standard deviation, test the difference between the two groups statistically by t-test or presented as a percentage and test the difference between two groups are statistically equal to Chi-square test.
- Compare values of one quantitative variable across different groups by analysis of variance (ANOVA).
- The difference is statistically significant when the confidence interval is > 95% (p < 0.05).
- Patient was explained and consulted about the willingness to cooperate in research.
- Instructions for signing voluntary research cooperation papers for patients who agree to participate in the research.
- All patients are examined, prescribed treatment and attentive care.

3. MAIN RESULTS

3.1 Common Features of Subject

Female patients accounted for 58.6%; patients ≥ 60 years old account for 66.6%. The mean age of the study group was 62.4 ± 9.3. There are 49.8% of overweight and obese patients, the average BMI of patients is 22.3 ± 1.9. The average time of detecting diabetes mellitus of the study subjects was 15.2 ± 8.6 years. There are 46.2% of patients with pre-hypertension status when measured at the clinic.

3.2 Characteristics of Maskedhypertension in Type 2 Diabetes Patients

When applying the JNC II hypertension grade with 186 patients with type 2 diabetes with MH, up to 98.9% increase in blood pressure level I, only 1.1% of patients with hypertension level II.

MH at night accounted for the highest rate, 43.0%.

Table 1. Common characteristics of subject (n = 186)

Features		Number	Ratio %
Gender	Male	77	41.4
	Female	109	58.6
Age (year)	≥ 60	124	66.6
	Min → max	38 → 82	
	Average	62.4 ± 9.3	
BMI	≥ 23	74	49,8
	Min → Max	16.5→30.6	
	Average	22.3 ± 1.9	
Time of diabetes discover (years)	> 5	118	63.4
	Min → max	1 → 22	
	Average	15.2 ± 8.6	
Characteristics of blood pressure when measured at the clinic	Normal	100	53.8
	Pre hypertension	86	46.2

Table 2. Rate of hypertension according to JNC II of study subjects (n = 186)

Level THA	Number	Ratio %
THA level I	184	98.9
THA level II	2	1.1
Total	186	100

Table 3. Characteristics of MH bodies of study subjects (n = 186)

	Number	Ratio %
MH 24 hours	61	32.8
MH day	45	24.2
MH night	80	43.0
Total	186	100

Table 4. Average blood pressure values of study subjects (n = 186)

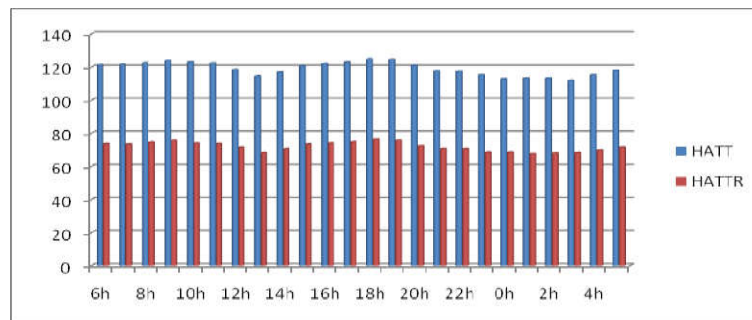| Average HA mmHg		Masked hypertension (mmHg) $\overline{X}$ ± SD
Day	Systolic blood pressure	128.4 ± 10.7
	Diastolic blood pressure	77.9 ± 6.8
Night	Systolic blood pressure	123.8 ± 9.8
	Diastolic blood pressure	75.2 ± 6.1
24 hours	Systolic blood pressure	126.9 ± 9.4
	Diastolic blood pressure	77.0 ± 6.0

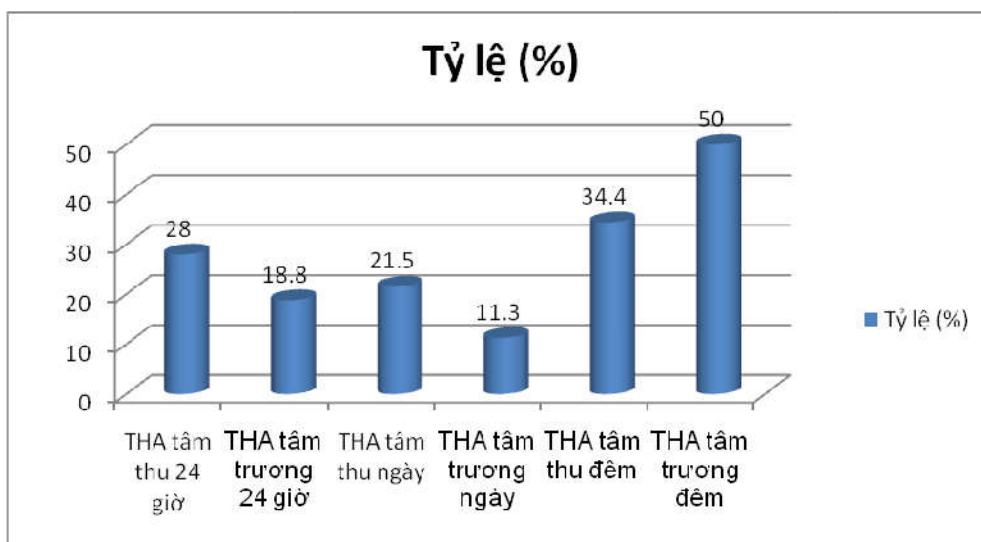**Fig. 1. Mean variation in systolic and diastolic blood pressure 24 hours according to ABPM (n = 186)**

Chart 1. Characteristics of MH by ABPM (n = 186)

Average nocturnal hypertension of study subjects exceeded the threshold for ABPM applied by the International Association of Hypertension (ISH-2003).

On average, the highest increase is around 9am and 19 pm, slightly down around 13 pm and down at the deepest around 2-3 am. There is a synchronous variation between systolic and diastolic blood pressure.

Hypertension concealed at night accounts for the highest percentage. 50% of 186 patients had nocturnal hypertension; 34.4% of patients had nocturnal hypertension.

3. DISCUSSION

4.1 Clinical Characteristics

After analyzing the results obtained in 186 type 2 diabetic patients with MH treated at Thai Binh Medical University hospital, we found that the percentage of female patients was dominant, 58.6%. The mean age of the study group was 62.2 ± 9.3.

Age and sex are two risk factors affecting the occurrence of some chronic diseases, including hypertension and type 2 diabetes. In middle age or old age, there will appear changes of some influencing factors that can then be the cause or pathogenesis of hypertension and type 2 diabetes such as insulin resistance, dyslipidemia, overweight, obesity, and metabolic disorders of

certain substances in the body. The frequency of both hypertension and diabetes increases with age. Age ≥ 60 is the age at which the likelihood of hypertension, type 2 diabetes is highly appropriate after eliminating cases of secondary hypertension, diabetes type 1, diabetes with causes [5].

The longer the time to detect diabetes, the higher the rate of complications. The higher the complication rate of the target organs, the less will the ability to adapt and compensate the patient's body in general to the nervous system and the cardiovascular system in particular. The above characteristics can affect the patient's blood pressure variability. According to our research results, diabetes time of more than 5 years accounts for a high rate of 63.4%. Research results Tran Huu Tram Em (2008) in over 80 patients with type 2 diabetes inpatient treatment reported the detection time of the disease from 5 to 10 years, accounting for the highest percentage [6].

Being overweight, obesity is always a risk factor for the occurrence of both hypertension and type 2 diabetes, possibly a more expressed role in type 2 diabetes. In our research group BMI on average 22.3 ± 1.9, the rate of patients are overweight 26.9%, obesity 12.9%. Our results are not much different from domestic and foreign studies. Vo Thi Ha Hoa [7], a study on 36 diabetic patients, recorded an average BMI of 23.7 ± 2.16 patients with the rate of overweight and obesity accounting for 63.9% [7]. Ohasama's

study showed that BMI in patients with type 2 diabetes was 22.7 ± 2.9 [8].

Our study subjects have blood pressure readings at the clinic <140/90 mmHg. The mean systolic blood pressure of study subjects was 114.4 ± 10.19 mmHg and the mean diastolic blood pressure was 69.5 ± 7.7 mmHg, the highest blood pressure was 135/85 mmHg. This is consistent with the standards of the study subjects. In 186 study patients when graded according to JNC VII, the rate of our hypertension level I accounted for 98.9%, level II hypertension 1.1% and the type of hypertension at night. This explains the frequent occurrence of left ventricular thickening and nocturnal stroke in type 2 diabetes patients.

4.2 Characteristics of Masked Hypertension in Type 2 Diabetes Patients

We surveyed 186 diabetic patients with normal blood pressure, after carrying ABPM, there are features: blood pressure increases in the morning from 7:00 to 10:00 and in the afternoon from 16:00 to 19:00, blood pressure drops from 12:00 to 14:00 o'clock and from 0:00 o'clock to 3 o'clock. Our results are similar to those of domestic and foreign studies. In the study of Vo Thi Ha Hoa, there are 2 ranges of hypertension in 24 hours (at 7:00 to 9:00) and at 16:00 to 19:00 and there are 2 ranges of blood pressure decrease at 12:00 to 14:00 o'clock and from 0:00 to 3:00 o'clock [9]. The physiological rate of blood pressure during the day and night usually fluctuates with a peak of BP around 9am and 7pm, a slight drop around 13 pm and the deepest drop around 2-3 am, The range is also typically around 10% relative to mean daytime blood pressure.

Until now, the assessment of blood pressure status, assessing the effectiveness of blood pressure control mainly based on measuring blood pressure in the clinic. When examining ABPM to get 186 patients with type 2 diabetes with MH, we needed to monitor blood pressure in 326 patients, so the incidence of MH was recorded in 57.0% of cases. This finding shows that the rate of MH in type 2 diabetic patients is very high. The results of this study are equivalent to the results of other studies at home and abroad. According to Nguyen Tran Tuyet Trinh, the rate of MH accounted for 57.8% in type 2 diabetic patients with controlled hypertension and 52.1% in patients with type 2 diabetes without

hypertension [10]. The MH status of our study was higher because Nguyen Tran Tuyet Trinh's study subjects surveyed type 2 diabetic patients who did not have hypertension with BP <130/80 mmHg.

Even so, there is a consensus among studies with the view that MH accounts for a high proportion in type 2 diabetic patients. In an analysis of 1,332 patients 40 years of age and older in Japan , the authors discovered that the rate of MH was 17.0% [11]. In 2012, a study in Da Nang conducted a study on the characteristics of MH with ambulatory blood pressure on 55 patients aged 35-80 recorded a rate of MH of 30.9%. These studies all examine the MH situation from the general population (Bendov et al., 2005). On the contrary, studies evaluating MH in type 2 diabetic patients, this rate ranges from 8 to 57.2%. In 2007, Marchesi studied 71 patients with type 2 diabetes and concluded that MH accounted for 47.0% [11]. The rate of MH in this community was equivalent to that of the study group of patients with type 2 diabetes in Japan 46.9%. Meanwhile, Cloutier L. et al. Noted that the MH rate was only 13.4% (Bendov et al, 2005).

Type 2 diabetes is an underlying risk factor for high blood pressure. For example, the Finn - Home study examining MH risk factors concluded type 2 diabetes was an independent risk factor for MH and increased its risk by eight times with a group of patients without diabetes [2]. This is again confirmed in the study, diabetes increases the risk of MH by 3.4 times. The rate of MH in each study was different depending on the means of diagnosis, diagnostic criteria for MH and the population of patients included in the study with different risk factors. On the other hand, it suggests that MH may be present in type 2 diabetic patients whose clinic blood pressure is clearly normal. The high frequency of MH becomes of concern when we consider that this condition may be associated with a higher risk of brain and kidney damage and may also be associated with heart damage, further increasing the risk. Very high availability for typical cardiovascular complications for diabetics.

ABPM measures blood pressure readings over many times of a day. Blood pressure index measured by this method is used to diagnose hypertension, but it is effective in monitoring the variation in blood pressure over time, day-night rate. This information is very valuable as a basis

for assessing the degree of blood pressure control under the impact of treatment measures. Based on the 24-hour blood pressure index it can be found that the variation in blood pressure over time is an important basis for the prognosis of the disease, for the use of drugs and the application of appropriate preventive measures for complications.

In patients with type 2 diabetes, the rate of hypertension at night is higher. The phenomenon of only hypertension at night is related to the activity of the autonomic nervous system of the heart. In type 2 diabetes patients, when hypertension occurs, there will be an increase in sympathetic nerve activity instead of the normal state that increases the activity of the parasympathetic nerve. Consequently, both diastolic and nocturnal hypertension are associated with abnormal functioning of the autonomic nervous system. Both of these events pose a high risk of developing complications due to spikes in diastolic blood pressure or nocturnal hypertension. The above changes in the 24-hour BP index above are mainly related to autonomic nervous system dysfunction due to type 2 diabetes. Type 2 is a day-night BP arrhythmia, which is a nocturnal hypertension phenomenon that often does not accompany clinical symptoms, thus making it difficult to recognize both from the patient and the practitioner in clinical practice. That also explains why in high blood pressure patients in general, complications such as paroxysmal hypertension, cerebral hemorrhagic stroke, acute or nocturnal pulmonary edema increase morbidity and mortality of the patient [5].

One advantage of ABPM in diabetic patients is particular concern for its ability to detect day-and-night blood pressure changes that are characteristic of the medical condition. In particular, no nocturnal hypertension or even reverse dipping (reverse dipping) was common in this population, with a frequency of about 30.0%. This figure suggests that the condition may reflect autonomic dysfunction, and some authors suggest that they may be used as clinical indicators of diabetic autonomic neuropathy. However, other pathophysiological mechanisms may also be involved. Sleep apnea, in particular, is common in obese people with type 2 diabetes, a condition commonly associated with non-depressive nocturnal blood pressure.

The 24-hour blood pressure variation in patients with MH has 2 ranges of increase and decrease in blood pressure. This is one of the risk factors for cardiovascular complications. Our study recorded the mean variation in blood pressure over 24 hours ranged at 122.18 ± 12.4 mmHg and the maximum amplitude of variation was 21.3 mmHg, with the mean highest blood pressure at 18:00 – 19:00 o'clock at 132/80 mmHg and lowest at 3:00 o'clock at 120/74 mmHg. This result shows that the MH subject should be given the same attention as the subject with real THA.

In addition to day-night blood pressure changes, monitoring of ABPM can provide information with other characteristics of blood pressure variability that may be of benefit in diabetics and of clinical significance. One of these is the overall blood pressure variability, usually manifested by the standard deviation of the 24-hour blood pressure, daytime and nocturnal blood pressure values.

This parameter is often increased in diabetics, which may indicate a disorder of automatic control of circulation and/or an increase in arterial wall stiffness. This is true in patients with diabetic autonomic neuropathy, especially when associated with impaired arterial pressure reflexes and may be an independent predictor of cardiovascular complications. Autonomic neuropathy is often associated with postprandial hypotension, a specific component of the 24-hour blood pressure fluctuation that can also be detected by ABPM. Another important feature of 24-hour blood pressure is early morning blood pressure behavior. Both early morning spikes (increased with morning awakening) and morning hypertension (blood pressure that rises during several hours in the morning) are associated with an adverse prognosis in diabetics. Early morning hypertension is common in diabetics and shows a prediction of diabetic neuropathy progression. Several studies now show that high blood pressure in the early morning hours is associated with an increased risk of stroke and heart attack in the early hours of the morning. Although studies so far in diabetic patients, home blood pressure monitoring is used to evaluate early morning blood pressure behavior, ABPM gives better results, once it allows for evaluation of kinetics and limb dynamics more than blood pressure in the morning hours [12].

5. CONCLUSION

Through analysis of 186 patients with type 2 diabetes with masked hypertension with 41.4%

men, 58.6% women, average age 62.4 ± 9.3 years we see: 98.9% of patients with hypertension level I, only 1.1% of patients with hypertension level II; Masked hypertension at night accounted for the highest proportion of 43.0%, of which the average systolic blood pressure was 123.8 ± 9.8 mmHg, and diastolic blood pressure was 75.2 ± 6.1 mmHg; On average, the highest increase is around 9am and 19pm, slightly down around 13pm and down at the deepest around 2-3am. There is a synchronous variation between systolic and diastolic blood pressure and have nocturnal hypertension at night.

6. RECOMMENDATIONS

It is necessary to measure blood pressure 24 hours with an automatic carry-on device for type 2 diabetes patients to detect hidden hypertension, from which to see the blood pressure characteristics in these patients to work out on suitable care strategy.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

The study is beneficial for patients and has been unanimously agreed by the Ethics Council of Thai Binh University of Medicine and Pharmacy, Vietnam.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. William BW. Ambulatory blood-pressure monitoring in clinical practice. NEJ M. 2013;348(24):2377–2379.

2. Charvat J, Chlumsky J, Szabo M. The association of masked hypertension in treated type 2 diabetic patients with carotid artery IMT. Diabetes Research and Clinical Practice. 2010;89: 239–242.

3. Cloutier L, Lamarre-Cliche M. Hypertension in adults with type 2 diabetes: A review of blood pressure measurement methods, targets and therapy. Canadian Journal of Diabetes. 2018;42(2):188–195.

4. ESC/ESH Guidelines for the management of arterial hypertension, Eur Heart J; 2018.
    DOI: 10.1093/eurheartj/ehy339

5. Nguyen Hai Thuy. Pathogenesis of hypertension in diabetic patients, Medical Publishing House, Hanoi; 2011.

6. Nguyen Huu Tram Em. Survey blood pressure circadian rhythm using technique of 24-hour blood pressure monitoring (ABPM). Proceedings of the full text of scientific topics, the ninth National Heart Congress, Journal of Cardiology. 2002; 29(2):100–110.

7. Vo Thi Ha Hoa, Dang Van Tri. Study on some characteristics of hidden hypertension detected by 24-hour ambulatory blood pressure at Hospital C Danang. Journal of Endocrinology – Diabetes. 2012;8:725–733.

8. Asayama K, Sato A, Ohkubo T. The association between masked hypertension and waist circumfernce as an obesity-related anthropometric index for metabolic syndrome: The Ohasama study. Hypertension Research. 2009;32(6):438–443.

9. Vo Thi Ha Hoa. Investigation of blood pressure variability in patients with hidden hypertension via the 24-hour blood pressure holter. Journal of Practical Medicine. 2014;918:118–124.

10. Nguyen Tran Tuyet Trinh. Survey of hidden hypertension in type 2 diabetes patients, Thesis of resident doctor, University of Medicine and Pharmacy, Ho Chi Minh City; 2013.

11. Marchesi C, Maresca AM. Masked hypertension in type 2 Diabetes mellitusrelationship with left-ventricular structure and function. Am J Hypertens. 2007;20(10):1079–1084.

12. Huynh Van Minh. Hidden hypertension. Proceedings of the XII National Heart Conference; 2010.