# THE COEXISTING CARDIOVASCULAR RISK FACTORS IN ELDERLY HYPERTENSIVE PATIENTS AT KHANH HOA IN VIETNAM

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**ABSTRACT**

***Background***: *Although, there is a progressive decline in cardiovascular mortality in North America, West Europe, Japan and Australasia, but most hypertensive subjects have imperfect control. In addition, the prevalence of hypertension in Vietnam as well as in developing countries is notable increasing along with the total numbers of strokes and coronary heart disease (CHD) events*

***Objective***: *The aim of this study is to determine the cardiovascular risk factors associated with hypertension and the application of the new WHO/ISH guidelines on clinical practice at Khanh Hoa Province, Vietnam.*

***Subjects and Methods:*** *Cross-sectional study, 258 hypertensive patients with age older than 60 (140 males and 118 females, mean age: 70.37±7.69) were defined according to the 1999 WHO/ISH criteria. Blood pressure was measured on the right arm with a mercury sphygmomanometer by a physician or a trained nurse. All subjects were evaluated their risk factors by a comprehensive clinical history and full clinical examination. An electrocardiogram at rest and blood samples were obtained after an overnight fast and analyzed for total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides, glycemie, and creatinine. In case of total cholesterol >2g/l, HDL-C > 35mg/dl, LDL-C >130mg/dl and glycemia >126mg/dl, a second blood sample was taken to define for the hypercholesterolemia and diabetes mellitus. Assessment of risk level is calculated according to the criteria of 1999 WHO/ISH guidelines.*

***Results:*** *The prevalence of isolated systolic hypertension was 36.04 per cent. The mean summation of major risk factors per individual was 1.5 ± 0.82 with 1.89 ± 0.81 (male) and 1.05 ±0.58 (female) P<0.001. The results of additional risk factors were as followed: Hypercholesteroemia 49.41%. (10.89% >2.5g/l). Smoking: 29.45%. Diabetes mellitus: 21.17 %. Family history of premature cardiovascular disease (CVD): 5.81 %. HDL-C < 35mg/dl: 51.51 %. LDL –C >130mg/dl: 46.66 %. Obesity: 1.62 %. Overweight: 12.60 %. Left ventricular hypertrophy: 18.29 %. Microalbuminuria / diabetes 25.92 %. Cerebrovascular disease: 10.07 %. Heart disease: 11.62 %. Renal disease: 3.48 %. Hypertension with grade 1: 35.82 %, grade 2: 42.63 %, grade 3: 20.54 %. Compared with the number of risk factors in the International Nifedipine GITS Study: Intervention as a Goal in Hypertension Treatment (INSIGHT) and the Antihypertensive Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), there was no significant difference. The rate of stratifying risk to quantify prognosis (of the typical 10-year risk of stroke or myocardial infarction) with "Low- risk": 2.32 per cent, "Medium- risk": 39.62 %, "High- risk": 25.96 %, " Very- high-risk": 41.08 %. The application of the current guidelines by local medical practitioners was still very modest.*

***Conclusion:*** *Cardiovascular risk assessment is an important addition to the doctor's diagnostic and prognostic black bag. However, this study showed that there was little evidence that the clinical practice has improved following release of guidelines. The guidelines were widely acknowledged but largely ignored. Therefore, we need to have univesary guideline and the strategies to apply better theses guidelines for management of hypertension as well as of other risk factors in clinical practice with optimal treatment to improve the quality of life of patient: live longer, live healthier, live happier.*

**Key words**: cardiovascular, coronaryheart disease, isolated systolic hypertension

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## INTRODUCTION

The second haft of the twentieth century saw a progressive decline in cardiovascular mortality in North America, West Europe, Japan and Australia[1, 2]. However, the percentage of persons in whom hypertension was controlled (defined as a systolic blood pressure (SBP) of less than 140 mmHg and a diastolic blood pressure (DBP) of less than 90 mmHg) is widely viewed as unsatisfactory. The rate of uncontrolled high blood pressure in the United States, Canada, England and France was 27%, 16%, 6% and 24% respectively. For the countries such as Finland, Australia, Germany, Scotland and India (which the criteria of controlled hypertension are defined as a systolic blood pressure of less than 160 mmHg and a diastolic blood pressure of less than 95 mmHg) these proportions were 20.5%, 20%, 19%, 22.5%, 17% and 9 % respectively[3-4].

However, the prevalence of hypertension in Vietnam as well as in developing countries is notably increasing along with the incidence of strokes and coronary heart disease (CVD) events[1-7]. The prevalence of hypertension in the Asia-Pacific region was from 11% to about 35%[6]. Some of these differences are probably attributable to differences in methodology, demographic composition and socio-economic circumstances[5-6]. In Vietnam, a national epidemiology study of hypertension by the Vietnam National Heart Institute was carried out in 1990. The results showed the prevalence of hypertension was 11% (BP≥140/90mmHg)[7] and the prevalence in Khanh Hoa province was 9%[8]. For the city of Hanoi itself, the prevalence of hypertension was 16.09%[9] in 1996, 18.69% in 2000 was and 23%[10] in 2002. In Thailand, a second national survey was carried out in 1996 and showed a prevalence of 11.6%. The result of Bangkok city was 13,4% (1996) and 23% in the 2000 survey [11]. In South Korea, the prevalence of hypertension (BP≥140/90mmHg) in males and females was 22% and 23% (1990), 31% and 27% in 1998[12] respectively.

In the recent years, the new wave guidelines for the management of individual risk factors were released (Table1). However, nobody have a clear view about the effectiveness of these guidelines on how physicians at the front line practice. In order to give a partial answer to the above problem, we conducted a study with the goals of (1) determining the coexisting cardiovascular risk factors with hypertension according to the new WHO/ISH criteria, and (2) to assess the application of these guidelines in clinical practice by local physicians at Khanh Hoa Hospital, Vietnam.

Table 1: Guidelines released by Cardiovascular Societies

1. The third Adult Treatment Panel ATP III of the National Cholesterol Education Program (NCEP May/2001)[13 14],
2. The American Diabetes Association ADA 2001 Clinical Practice Recommendation Diabetes Care[15],
3. The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High blood Pressure (JNC VI 1997)[16],
4. The Recommendations of the Second Joint Task Force of European and other Societies on Coronary Prevention (ESCP II 1998)[17],
5. The Guidelines for management of hypertension: report of the third working party of the British Hypertension Society (BHS III 1999)[18],
6. The 2000 Canadian Recommendations for the Management of Hypertension (CANADA 2000)[19],
7. The World Health Organization-International Society of Hypertension (WHO/ISH) Guidelines for the Management of Hypertension (WHO-ISH 1999)[1],
8. The Assessment of Cardiovascular Risk by Use of Multiple-Risk-Factor Assessment Equations American Heart Association/American College of Cardiology (AHA/ACC) Scientific Statement 1999[20],
9. The AHA/ACC Guidelines for Prevention Heart attack and death in Patients with Atherosclerotic Cardiovascular disease: 2001 Update[21]etc...

## METHODS

### Subjects and Study Design

The patients in the study were prospectively recruited from the department of cardiology and geriatrics at Khanh Hoa Hospital in Vietnam between May 2000 and May 2001. The cross-sectional study included 258 patients older than 60 (140 male and 118 female, mean age: 70.37±7.69) with hypertension as defined according to the 1999 WHO/ISH criteria. The diagnosis of hypertension was based on the average of two or more readings taken at each of two and more visits after the initial screening of systolic blood pressure (SBP) equal or above 140 mmHg and/or a diastolic blood pressure (DBP) of 90 mmHg or more. Isolated systolic hypertension (ISH) is defined as a SBP of 140mmHg or more and a DBP of less than 90 mmHg. The blood pressure (BP) was measured at rest on the right arm by a physician or a trained nurse with a mercury sphygmomanometer, with the patient sitting and his/her arm supported at level of heart. All patients with secondary hypertension were excluded.

**Risk Factor Assessment**

All subjects were evaluated for risk factors by answering a standard questionnaire and undergoing a complete clinical examination. Body weight and height were recorded. Body mass index (BMI) was computed as weight divided by height squared. An electrocardiogram at rest and blood samples were obtained after an overnight fast and analyzed for total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides, glycemie, and creatinine by the Cobas Miras apparel (Roche, Germany). . If the total cholesterol level was >2g/l, HDL-C > 35mg/dl, LDL-C > 130mg/dl and glucose > 126mg/dl, a second blood sample was taken to confirm the diagnosis of hypercholesterolemia or diabetes mellitus.. The Risk assessment was calculated according to the criteria of 1999 WHO/ISH. All subjects were evaluated for target organ damage, other cardiovascular risk factors, and conditions that may influence treatment. The severity of hypertension was classified as grade I, grade II and grade III. Other factors influencing prognosis include A/Risk factors: men > 55 years, women> 65 years, cigarette smoking, total cholesterol >6.5 mol/l, diabetes mellitus, family history of premature of CVD. B/ Target organ damage: left ventricular hypertrophy (electrocardiogram, echocardiography, chest X-ray), proteinuria with slight elevation serum creatinine, atherosclerotic plaque by ultrasound/ X-ray, retinopathy (grade II). C/ Associated clinical conditions: Cerebrovascular disease, heart disease, renal disease, vascular disease, advanced retinopathy. The stratification of patients by absolute level of cardiovascular risk is showed in Table 2.

Table 2 Stratifying risk to quantify prognosis

| | **Blood pressure (mmHg)** | | |
|---|---|---|---|
| **Other risk factors and disease history** | **Grade 1** (mild hypertension ) SBP 140-159 or DBP 90-99 | **Grade 2** (moderate hypertension) SBP 160-179 or DBP 100-109 | **Grade 3** (severe hypertension) SBP ≥ 180 or DBP ≥ 110 |
| **I. no other risk factors** | Low risk | Medium risk | High risk |
| **II. 1-2 risk factors** | Medium risk | Medium risk | Very high risk |
| **III. 3 or more risk factors or TOD or diabetes** | High risk | High risk | Very high risk |
| **IV. ACC** | Very high risk | Very high risk | Very high risk |

TOD= target organ damage; ACC = associated clinical conditions, including clinical CVD or renal disease. The typical 10-year risk of stroke or myocardial infarction is shown, where 'low risk' corresponds to below 15%, 'medium risk' to 15-20%, 'high risk' to20-30%, and 'very high risk' to 30% or higher[1].

We also assess the awareness of the guidelines by local practitioners, and the application of these guidelines in their clinical practice. In addition, we also compute the different classes of drug prescribed for the hypertensive patients.

**Statistical Analysis**

Data were expressed as mean ± SD. Differences between two sexes were assessed by Student's t test for continuous variables. The relation between hypertension and risk factors were analyzed of correlation by

using Pearson correlation coefficient. Value of $P < 0.05$ was considered significant. Data were analyzed with SPSS 10.0 for Window (SPSS Institute. Chicago, Illinois)

**RESULTS**

The baseline characteristics of men and women in the study are presented in the Table 3. The ratio of male/female was 1.18. The mean age was 71 years (range 64-78 years). The prevalence of ISH was 36.04 %( Figure 1).The mean summation of major risk factors per individual was 1.5 ± 0.82 with 1.89 ± 0.81 in male and 1.05 ±0.58 in female (P<0.001). The percentage of additional risk factors included: Hypercholesterolemia (>2 g/l): 49.41 % (>2.5g/l: 10.89%), Smoking: 29.45 %, Diabetes mellitus: 21.17%, Family history of premature CVD: 5.81 %, HDL-C < 35mg/dl: 51.51 %, LDL –C >130mg/dl: 46.66%, Obesity: 1.62 %. Overweight: 12.60 %, Left ventricular hypertrophy: 18.29 %, Microalbuminuria /diabetes: 25.92 %, Cerebrovascular disease: 10.07 %, Heart disease: 11.62 %, Renal disease: 3.48 % (Figure 2), and Hypertension with grade 1: 35.82 %, grade 2: 42.63 %, grade 3: 20.54 % (Figure 3).

Table2. Some baseline characteristics of hypertensive patients between men and women

| | Mean ± STD | Male ± STD | Female± STD | Value P |
|---|---|---|---|---|
| Age | 71.89 ±7.69 | 70.87±6.72 | 71.56±8.08 | 0,456 |
| Weight (kg) | 52.86 ± 10.61 | 56.84±10.14 | 48.29±9.23 | 0.0001 |
| Height (m) | 1.56 ± 0.07 | 1.61±0.05 | 1.51±0.05 | 0.0001 |
| BMI | 21.46± 4.75 | 21.79±3.41 | 21.08±3.99 | 0.13 |
| Systolic (mmHg) | 164.69±17.20 | 166.37±16.86 | 162±17.47 | 0.08 |
| Diastolic (mmHg) | 90.58±9.19 | 92.03±9.07 | 88.85±9.06 | 0.005 |
| Mean BP (mmHg) | 115.28±10.24 | 116.81±9.73 | 113.47±10.57 | 0.009 |
| Total cholesterol (mg/dl) | 202.18±45.06 | 213.64±51.19 | 188.68±31.80 | 0.0001 |
| Glucose (mg/dl) | 113.92±49.6 | 108.81±36.69 | 120.05±61.24 | 0.07 |
| LDL-Cholesterol (mg/dl) | 125.93 ±37.2 | 133.87±42.9 | 122.71±34.2 | 0.92 |
| HDL-Cholesterol (mg/dl) | 37.78±19.93 | 40.81±15.75 | 36.55±21.34 | 1.96 |
| Triglyceride (mg/dl) | 175.80±110.67 | 169.71±121.10 | 182.84±97.30 | 0.34 |
| Mean risk factor number | 1.5±0.82 | 1.89±0.81 | 1.05±0.58 | 0.0001 |
| Mean hypertension grade | 1,83±0.74 | 1.87±0.69 | 1.79±0.79 | 0.42 |
| Mean risk group | 3.06±0.90 | 3.04±0.87 | 3.08±0.94 | 0.76 |

There was a negative correlation between the BMI with the age r (2): -2.38 P<0.01. There was no correlation between the summations of risk factors with the mean BP. (Figure 4). The rate of stratifying risk to quantify prognosis (of the typical 10-year risk of stroke or myocardial infarction) with “Low risk”: 2.32 %, “Medium risk”: 39.62 %, “High risk”: 25.96 %, “ Very high risk”: 41.08 % (Figure 5). The application of the current guidelines for medical practitioners at local was very modest. Most of hypertensive patients were not assessed about for risk stratification. The proportions of the drug use were seen in Figure 6. There was no large difference when compared with the patient population of the INSIGHT and ALLHAT trials (Figure 7). The proportions of patients with one, two, three and more additional risk factors were 54 %, 36 %, 7 % and 2% respectively (Figure 8).

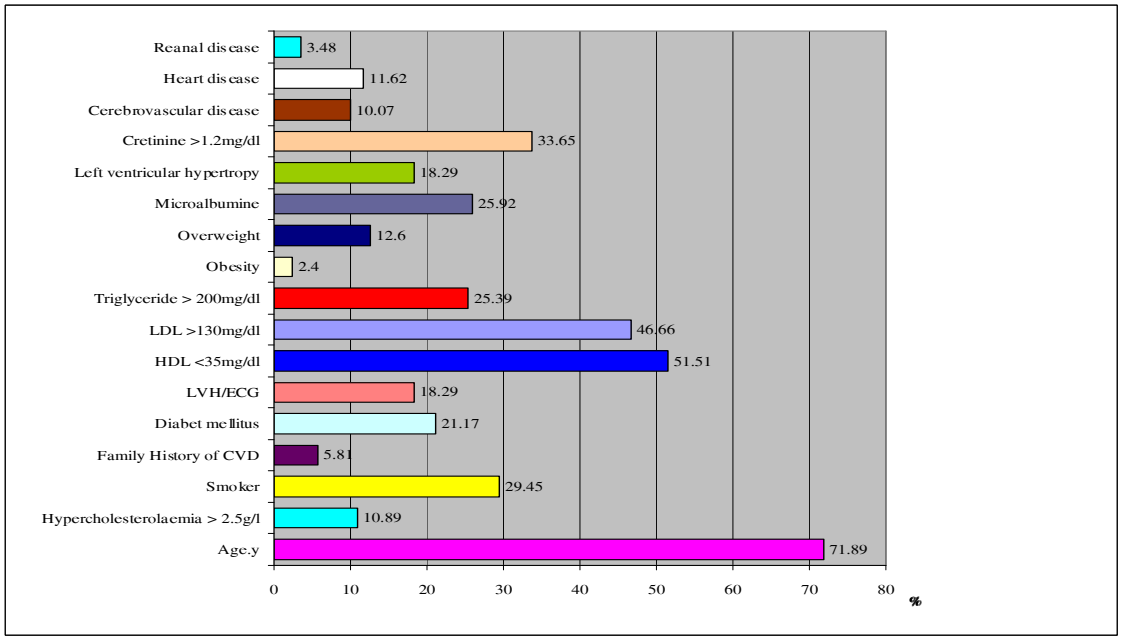


Figure 2. The coexisting cardiovascular risk factors with hypertension

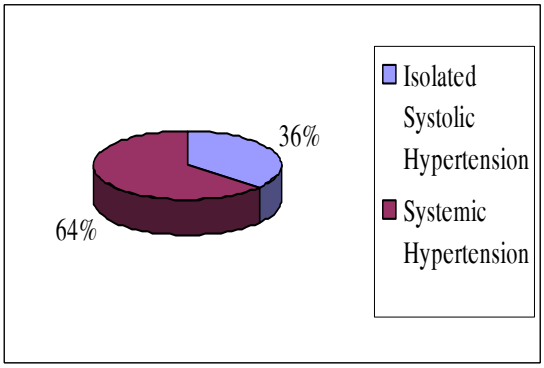


Figure 1. The prevalence of ISH

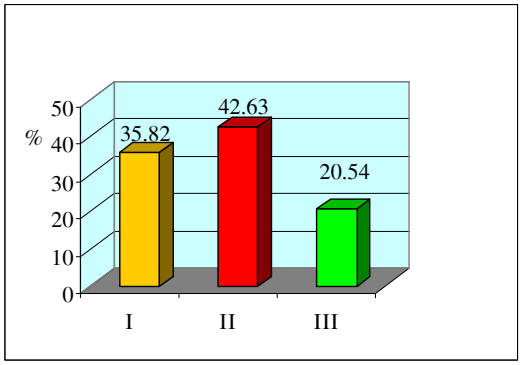


Figure 3. Classification of hypertension

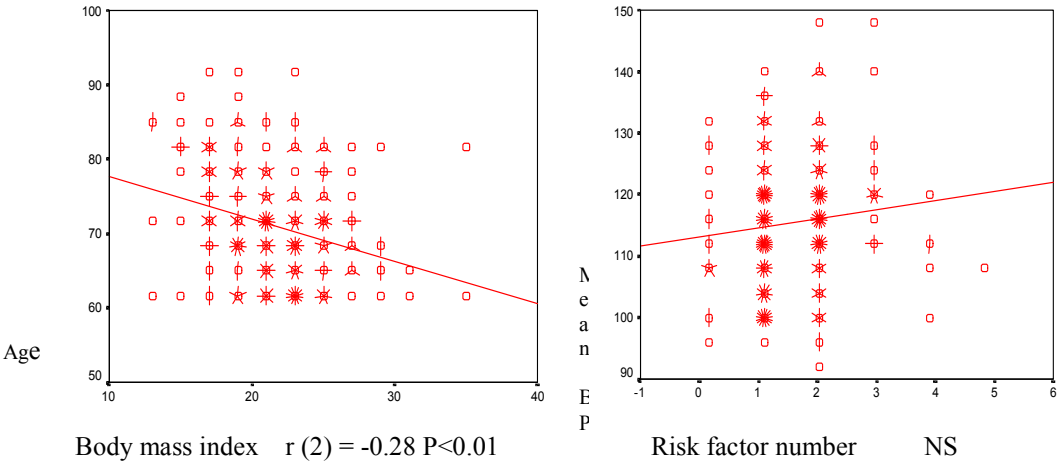


Figure 4 Relation between the age & BMI, mean BP & number of risk factors

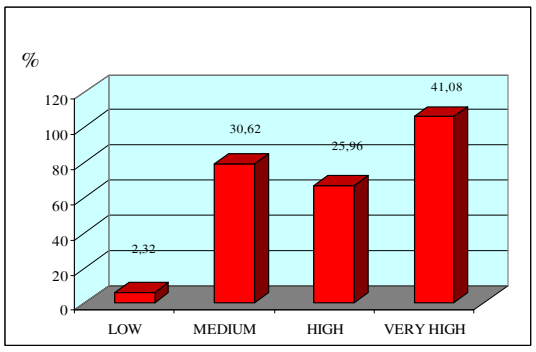


Figure 5. Stratifying Risk to Quantify Prognosis.

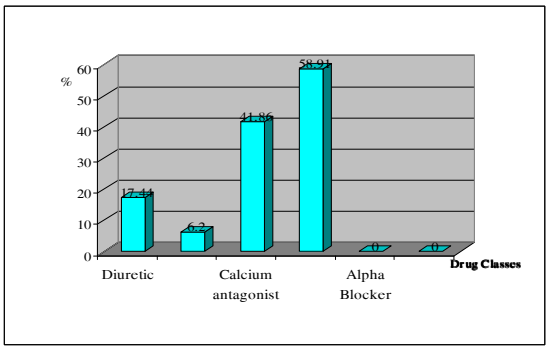


Figure 6. Proportion of the classes of drug were used

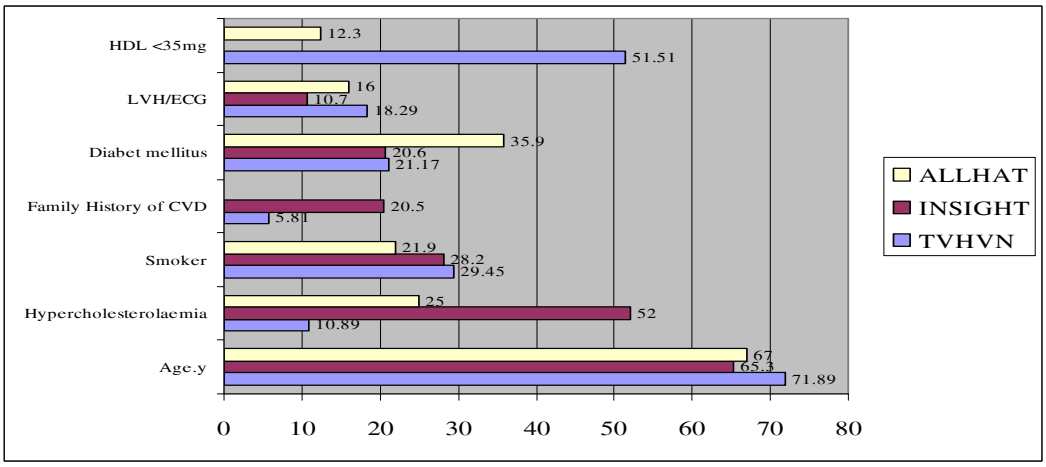


Figure 7. Compare the additional risk factors of ALLHAT & INSIGHT with our study (TVHVN)

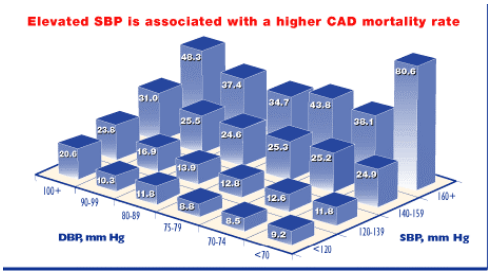


Figure 9 Multiple Risk Factor Intervention Trial

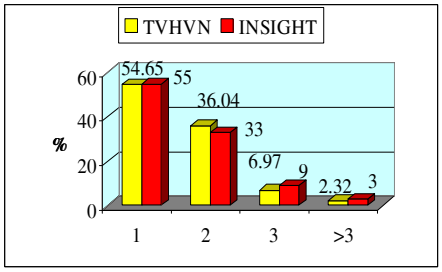


Figure 8 Proportions of patients with one, two, three or more additional risk factors

## DISCUSSIONS

### Role of Isolated Systolic Hypertension.

Population-based long-term follow up are urgently needed to demonstrate the association of risk factors with hypertension in Asia; however, prevention programs should be started based on cross-sectional surveys and cases studies without waiting for cohort studies[5]. Therefore, we realized that in the present study, the prevalence of ISH at elderly hypertensive patients was 36 % but most practitioners usually missed since they only diagnosed as simple hypertension. Nevertheless, over the past four decades, numerous studies have examined the influence of drug treatment of hypertension on the risk of cardiovascular events. The average

reduction in DBP of 5-6 mmHg in these trials conferred a reduction of about 38% in stroke incidence, a 16% reduction in CHD events, a 21% reduction in all vascular events and a 12% reduction in all-cause mortality[22]. However, nowadays, the role of ISH is especially important. The recent observational epidemiological studies and randomized controlled trials have demonstrated that SBP is an independent and strong predictor of risk of cardiovascular and renal disease[24]. The Multiple Risk Factor Intervention Trial (MRFIT) was a randomized, multicenter, primary prevention trial to assess the combined influence of BP, serum cholesterol level, and cigarette smoking on death from CAD. Data on risk factors were available for 316,099 white men aged 35 to 57 with no prior history of MI or diabetes after an average follow-up of 12 years has shown that SBP is a better indicator of increased risk of coronary artery disease than DBP[23]. A review 10 randomized trials with a total of 18.542 participants, antihypertensive treatment was associated 21% reduction in total (fatal and non-fatal) CHD events and 37% reduction in fatal stroke. An average reduction of 14-15 mmHg in SBP over 4 years confers 21% reduction in CHD, 37% reduction in stroke, 25% reduction in total cardiovascular mortality and 13% reduction in all-cause mortality[24-26]. J A Staessen et al reviewed the results of the three outcome trials in older patients with ISH (SHEP, SYST-EUR, SYST-CHINA) were pooled. Overall, active treatment reduced all-cause mortality by 17% and cardiovascular mortality by 25% compared with placebo[25]. In the Framingham study, SBP was used in the scoring system in order to assess the absolute risk 10 years for hard coronary artery disease[13 14]. From the INDANA project steering committee, Stuart et al presented the calculation of risk of CVD with five years have also used SBP to calculate score in the 11 risk factors to quantify an adult's risk of death from CVD including stroke and CHD[28]. Therefore, we need to have an early attention and intervention about the ISH in the elderly for active treatment in daily clinical practice.

**Coexisting Risk Factors with Hypertension**

The mean summation of major risk factors was different significantly between Vietnamese males and females with $P < 0.001$ (Table 3). The proportions of patients with one, two, three and more additional risk factors were similar with INSIGHT (Figure 8). Does this issue explain the development of the 'second wave' epidemic of CVD that is flowing thought developing countries? Compared with the baselines of the addional risk factors of INSIGHT and ALLHAT, there was not much different[4, 29](Figure 7). In generally, our summation of risk factors was similar with the ones in the developed countries. The proportion of the family history of CVD was lower than in the INSIGHT (5.2 vs. 20) and the proportion of hypercholesterolemia was also lower than in both INSIGHT and ALLHAT. Possibly, these differences may explain why the incidence of stroke is higher than heart disease in Vietnam as well as in the South East ASIA[12]. This problem requires to study further future scrutiny. However, if the total cholesterol level were over 2 g/l, the proportion of hypercholesterolemia would be 49 %. The proportion of HDL-C < 35 mg/dl was 51%. According to the ATP III, HDL-C < 40 mg/dl is as the major and independent risk factor. In the Heart Protection Study, treatment with statins even in the subjects with LDL-C level < 100mg/dl have also decreased significant their cardiovascular mortality[30, 39]. Therefore, we must pay on more attention on these major risk factors in the hypertensive patients. For type II diabetes is now considered a cardiovascular disease more than a metabolic disease[31], the proportion of diabetes coexisting with hypertension was similar with the proportion in developed countries (Figure 7). Nowadays, ATP III raised persons with diabetes but without CHD to the risk level of CHD risk equivalent[13]. Both JNC VI and 1999 WHO/ISH placed the hypertensive patients who have diabetes into the very high-risk group with the goal of treatment of less than 130/85 mmHg[1, 16]. In Europe and Canada, the current recommendations for the diabetic patients without nephropathy are that BP be reduced to ≤ 130/80 mmHg and that DBP of <80 mmHg is deemed safe[17, 9]. While obesity and physical inactivity are defined as major risk factors by AHA, we noted the proportion of these risk factors were very low in our patients in comparison with the Western countries[32]. The other risk factors of uncertain significance such as homocyserine, lipoprotein a, fibrinogen, C-reactive protein and plasmin renin were not observed in this study.

**Application of Guidelines 1999 WHO/ISH on Clinical Practice.**

We noted the ratio of hypertension at the grade 3 was the lowest but as evaluated for stratifying risk, the ratio of the very-high-risk group was the highest. These are the preeminent points of these guidelines; differences in risk of CVD are determined not only by the level of BP, but also by the presence or levels of

other risk factors. The stratification of patients by absolute level of cardiovascular risk is very important to quantify prognosis and appropriate therapy; however, most clinicians have not evaluated adequately this problem.

Until now, we have had too many guidelines for assessment of cardiovascular risk factors[13-21]. In every guideline, there are major and independent risk factors identified, but they vary so much from one guideline to another [1, 13-20, 33]. There are also too many methods to calculate a patient's absolute cardiovascular risk (Framingham risk equations, CVD life expectancy model, Dundee coronary risk disk, PROCAM risk function, British regional heart study risk function etc…)[33]. Therefore, it is necessary for the World Heart Organization/World Heart Federation to have a common, universal guideline to assess the cardiovascular risk factors in order to have better application of the guidelines into the real world. It is difficult for the local physicians to confront the plethora of tremendous amounts of available information, which confuse the medical practitioners at the front line. Guideline should be simple, clear, evidence-based, effective, and easily applicable into routine daily practice. We need measures to improve adherence, which focus on the physician and medical office, the heath deliver system and the patient.

While the JNC VI and even JNCVII, which will be released in the next few months, continue to recommend a diuretic or beta-blocker as first-line therapy unless there are compelling or specific indications for another drug[38], the proportion of prescribing these classes of drug in Vietnam has been very limited. Is the pharmaceutical industry responsible for this problem? Thus, we need to pay more attention on different aspect of prescribing medications for hypertension such as effectiveness, lower side effect profile, simple regimen, affordability to the patients.

## CONCLUSION

Cardiovascular risk assessment is an important addition to the doctor's diagnostic and prognostic black bag. However, this study showed that there was little evidence that the clinical practice has improved. Guidelines are widely acknowledged but largely ignored. Therefore, we need to have a univesary guideline and the new strategies of better applying theses guidelines for management of hypertension as well as of other risk factors in clinical practice with optimal treatment to improve the quality of life of patient: live longer, live healthier, live happier.

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