

ORIGINAL ARTICLE

Impact of global risk assessment on the evaluation of hypertensive patients treated by primary care physicians in Korea (A Nation-Wide, Multi-Center, Observational, Cross-Sectional, Epidemiologic Study to Evaluate the Proportion of Cardiovascular Risk Factors in Korean hypertensive patients: WONDER study)

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Global cardiovascular risk evaluation and stratification is essential to identify high-risk hypertensive patients. However, it is uncertain how often the strategy is executed in real clinical practice. We sought to evaluate whether global risk evaluation might change the risk stratification in Korean hypertensive patients treated by primary care physicians. A total of 3109 hypertensive patients were analyzed. The mean age was 62.3 ± 11.3 years, and 1502 (48.3%) of the participants were male. The global risk evaluation revealed that 1862 patients (59.9%) were classified as having high- or the very high-risk. High-risk patients were older and obese, and had a male predominance, a longer duration of hypertension and a low HDL-cholesterol. The systolic and diastolic blood pressures (BP) were significantly higher in the high-risk group ($P < 0.0001$). However, combination antihypertensive therapy was more common in the low-risk group ($P = 0.0265$). A total of 2155 patients (69.3%) were reclassified into the higher or the lower-risk group by performing additional tests. In a multivariate logistic regression analysis, age, body mass index, BP, metabolic syndrome, left ventricular hypertrophy and chronic kidney disease were independent factors associated with risk reclassification with global risk evaluation. In conclusion, although the majority of hypertensive patients treated by the primary care physicians were in the high- or very high-risk group, their risk levels were not appropriately stratified. However, simple additional tests enhanced the risk evaluation of hypertensive patients. Accordingly, comprehensive cardiovascular risk stratification should be undertaken in all hypertensive patients.

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INTRODUCTION

Hypertension is a major threat to global health because of its high prevalence and subsequent risk of cardiovascular disease. Accordingly, treating hypertension to prevent or delay the development of cardiovascular disease remains an essential component of public health policy throughout the world.¹

The cardiovascular risk increases with the accumulation of other risk factors or target organ damage (TOD). Thus, accurate global risk evaluation has an important practical impact on the treatment strategies. In fact, the presence of a high- or very high-risk profile mandates immediate initiation of antihypertensive drug treatment

and may be an indication for more aggressive intervention on the associated risk factors and comorbidities. Furthermore, it has been reported that identifying and targeting the subset of patients who are at the highest risk improve the cost effectiveness of antihypertensive treatment for any degree of blood pressure (BP) reduction.²

Thus, risk factors and TOD must be actively screened and treated if cardiovascular health is to be improved. In this respect, the European Society of Hypertension-European Society of Cardiology, the Japanese Hypertension Society and the NICE guidelines highlight several approaches for the evaluation of risk factors and TOD.^{3–5} However, it is uncertain whether the minimum work-up recommended by the

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guidelines is fully performed in daily practice, especially by the primary care physicians.

Therefore, we performed a nationwide cross-sectional survey to investigate: (1) the risk profile of Korean hypertensive patients treated by primary care physicians; (2) whether additional tests for cardio-metabolic risk factors and TOD will change the risk stratification; and (3) which factors are associated with the reclassification of the cardiovascular risk in the hypertensive patients.

METHODS

Study population

Primary care physicians stratified according to the proportion of the residents and the prevalence of hypertension in each city or province were randomly selected, and survey letters were sent to the 274 primary care clinics selected nationwide. Of the invited physicians, 247 physicians in 230 clinics agreed to participate in this study.

Patients who met the eligibility criteria were consecutively enrolled at the participating sites. Eligible hypertensive patients older than 18 years who were diagnosed with essential hypertension before this survey were included in this study. Subjects with secondary hypertension or who have participated in other clinical studies were excluded.

Among the 3122 recruited cases, 13 patients were excluded (declined to participate ($n=5$), inadequate sample ($n=8$)). Finally, 3109 cases were analyzed. Informed consent was obtained from all subjects. There were no treatment changes related to study participation. This study was approved by the Institutional Review Board of Seoul National University Bundang Hospital.

Patient evaluation and BP measurement

All subjects were asked to complete a questionnaire to collect information on demography, lifestyle and the family history of cardiovascular disease. Anthropometrical data, medical history (such as cardiovascular disease, cerebrovascular disease and peripheral vascular disease), presence of TOD and antihypertensive medication were also recorded by the primary care physicians.

The preevaluation risk was determined by the physicians as low, moderate and high based on the medical records and clinical intuition.

BP was measured by the physicians using an electronic sphygmomanometer (OMRON MX-3, Omron Healthcare, Kyoto, Japan). BP was measured after the subject had been seated quietly for 5 min, with the arm of the subject supported at the heart level. The average of two consecutive measurements with a 5-min interval was used for the analysis.

A fasting blood sample was collected in the morning after at least 8 h of fasting. The blood samples were centrifuged and refrigerated at the examination site and then transferred in iceboxes to the central laboratory (Green Cross Reference Lab, Yongin, Korea) on the same day. Plasma glucose was measured using an enzymatic method (HITACHI 7180, HITACHI, Japan), and total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol and creatinine were measured using an auto-analyzer (ADVIA 1650, Bayer, Tokyo, Japan). Hemoglobin A1C was measured with a high performance liquid chromatography assay (Variant II TURBO, Bio-Rad, Hercules, CA, USA). Urine microalbumin was measured with immunoturbidimetric assay (Cobas integra 800, Roche, Mannheim, Germany). To compensate for variations in urine concentration in spot-check samples, we compared the amount of albumin in the sample against its concentration of creatinine (albumin/creatinine ratio).

The body mass index (BMI) was calculated as the weight (in kg) divided by the height (in m^2). The waist circumference was measured from the narrowest point between the lower borders of the rib cage and the iliac crest.

Finally, we reclassified the risk of participants according to the 2007 ESH/ESC guideline using the results of the additional tests.

Definition

Participants were considered to have diabetes if they were receiving insulin or oral hypoglycemic agents, or if the fasting blood glucose levels exceed 126 mg dl^{-1} .⁶ The glomerular filtration rate (GFR) was calculated using the Modification of Diet in Renal Disease equation and chronic kidney disease (CKD) was defined if the estimated GFR was less than 60 ml min^{-1} per 1.73 m^2 . Left ventricular hypertrophy (LVH) was evaluated with the Romhilt-Estes point score system (point 5).⁷ Microalbuminuria was defined if the albumin/creatinine ratio in a random urine sample was $\geq 22 \text{ mg g}^{-1}$ in men and $\geq 31 \text{ mg g}^{-1}$ in women.⁸

Statistical analysis

All statistical analyses were performed using SAS (version 9.1, SAS Institute, Cary, NC, USA). Continuous variables were expressed as the mean \pm s.d. and

Table 1 Stratification of cardiovascular risk according to 2007 ESH/ESC Guidelines

Other risk factors, OD or disease	Optimal	Normal SBP 120-129 or DBP 80-84	High normal SBP 130-139 or DBP 85-89	Grade 1 SBP 140-159 or DBP 90-99	Grade 2 SBP 160-179 or DBP 100-109	Grade 3 SBP ≥ 180 or DBP ≥ 110
No other risk factors	4 (0.1)	17 (0.6)	14 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
1-2 risk factors	88 (2.8)	155 (5.0)	128 (4.1)	53 (1.7)	5 (0.2)	3 (0.1)
3 or more risk factors, OD or DM	328 (10.6)	455 (14.6)	504 (16.2)	563 (18.1)	112 (3.6)	27 (0.9)
Established cardiovascular or renal disease	125 (4.0)	150 (4.8)	152 (4.9)	185 (6.0)	31 (1.0)	10 (0.3)

Risk group	N	
Average risk	35	Low risk group (N=406)
Low risk	371	
Moderate risk	841	Moderate risk group (N=841)
High risk	1179	High risk group (N=1862)
Very high risk	683	

Abbreviations: CV, cardiovascular; DBP, diastolic blood pressure; DM, diabetes mellitus, OD, organ damage, SBP, systolic blood pressure. A full color version of this table is available at the *Hypertension Research* journal online.

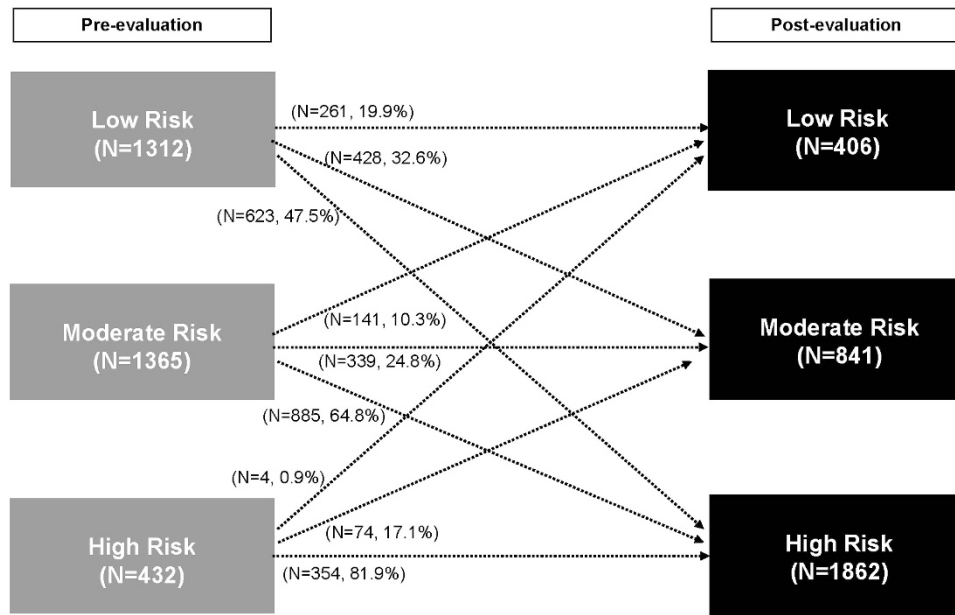


Figure 1 Distribution of hypertensive patients according to 2007 ESC/ESH guideline before and after global risk evaluation.

Table 2 Demographic and laboratory characteristics according to risk stratification

	Low risk (N = 406)	Moderate risk (N = 841)	High risk (N = 1862)	P-value
Age (years)	53.5 ± 8.2	63.4 ± 10.6	63.8 ± 11.3	<0.0001
Male gender, n (%)	159 (39.2)	372 (44.2)	971 (52.2)	<0.0001
BMI (kg m ⁻²)	24.9 ± 2.8	24.8 ± 3.2	25.3 ± 3.2	0.0018
Waist circumference (cm)	85.2 ± 8.2	87.7 ± 9.0	89.6 ± 8.9	<0.0001
Current smoker, n (%)	27 (6.7)	156 (18.6)	377 (20.3)	<0.0001
Family history of HT	213 (52.5)	398 (47.3)	907 (48.7)	0.2325
Duration of HT (years)	4.4 ± 4.3	5.8 ± 5.2	6.2 ± 6.0	<0.0001
SBP (mm Hg)	124.1 ± 8.8	120.5 ± 9.7	138.6 ± 14.6	<0.0001
DBP (mm Hg)	78.3 ± 6.3	74.2 ± 8.3	82.0 ± 10.4	<0.0001
LVH, n (%)	0 (0.0)	25 (3.0)	106 (5.8)	<0.0001
Diabetes mellitus, n (%)	0 (0.0)	219 (26.0)	544 (29.2)	<0.0001
Glucose (mg dl ⁻¹)	92.5 ± 17.2	106.7 ± 34.2	110.9 ± 40.1	<0.0001
Hemoglobin A1c (%)	5.7 ± 0.5	6.2 ± 0.9	6.3 ± 1.0	<0.0001
Cholesterol, total (mg dl ⁻¹)	184.4 ± 31.4	182.9 ± 35.6	183.0 ± 37.6	0.5544
HDL-cholesterol (mg dl ⁻¹)	49.4 ± 12.3	46.0 ± 11.7	46.4 ± 12.2	0.0006
LDL-cholesterol (mg dl ⁻¹)	106.7 ± 30.5	105.5 ± 31.9	105.2 ± 33.4	0.4458
Triglyceride (mg dl ⁻¹)	146.5 ± 90.7	160.2 ± 101.0	170.7 ± 108.0	<0.0001
BUN (mg dl ⁻¹)	15.1 ± 3.8	16.5 ± 4.6	16.7 ± 5.8	<0.0001
Creatinine (mg dl ⁻¹)	0.9 ± 0.1	1.0 ± 0.2	1.1 ± 0.3	<0.0001
Urine microalbumin (µg ml ⁻¹)	7.9 ± 5.0	23.1 ± 63.3	47.5 ± 132.3	<0.0001
Urine protein (mg dl ⁻¹)	9.6 ± 6.0	20.3 ± 201.5	20.1 ± 125.6	0.2775
Urine creatinine (mg dl ⁻¹)	120.0 ± 74.0	122.1 ± 78.1	115.6 ± 74.0	0.0818
Anti-HT medication, n (%)				
ACEI/ARB	55 (13.7)	127 (15.3)	333 (18.1)	
Beta-blocker	12 (3.0)	30 (3.6)	67 (3.7)	
Calcium channel blocker	47 (11.7)	113 (13.7)	283 (15.4)	0.0265
Diuretic	0 (0.0)	6 (0.7)	9 (0.5)	
Combination therapy	288 (71.6)	552 (66.7)	1145 (62.3)	

Abbreviations: ACEI/ARB, angiotensin converting enzyme inhibitor/angiotensin II receptor blocker; BMI, body mass index; BUN, blood urea nitrogen; DBP, diastolic blood pressure; HDL, high-density lipoprotein; HT, hypertension; LDL, low-density lipoprotein; LVH, left ventricular hypertrophy; SBP, systolic blood pressure.

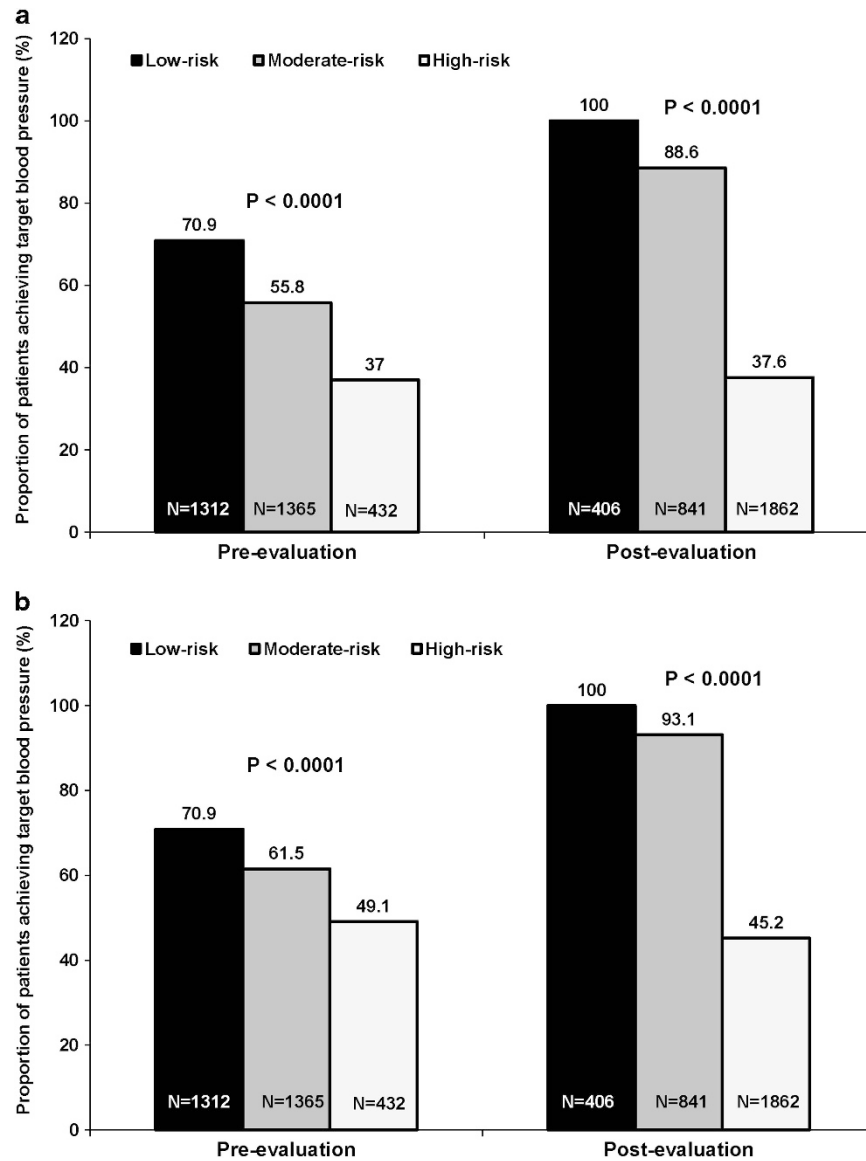


Figure 2 Control rate of hypertension before and after global risk evaluation and risk stratification. (a) Proportion of patients achieving target blood pressure (BP), BP goal < 130/80 mm Hg in patients with diabetes mellitus or chronic kidney disease, otherwise BP goal < 140/90 mm Hg. (b) Proportion of patients achieving target BP according to 2013 ESH/ESC guideline, BP goal < 140/85 mm Hg in patients with diabetes mellitus and BP < 130/80 mm Hg in chronic kidney disease patients with proteinuria, otherwise BP goal < 140/90 mm Hg.

compared using analysis of variance. Discrete variables were expressed as counts and percentages, and the Pearson's χ^2 -test or the Fisher's exact test was used to compare proportions. We performed logistic regression analysis to adjust for the factors that influence the risk reclassification. All statistical analyses were two-tailed, and *P*-values < 0.05 were considered statistically significant.

RESULTS

A total of 3109 hypertensive patients were analyzed. The mean age was 62.3 ± 11.3 years, and 1502 (48.3%) of the participants were male. The mean duration of hypertension was 5.9 ± 5.6 years. The mean systolic and diastolic BPs were $131.8 \pm 15.3/79.4 \pm 10.0$ mm Hg, respectively.

Global risk evaluation revealed that 1862 patients belonged to the high- or very high-risk group, who had LVH (106 patients, 5.7%), CKD (904 patients, 48.6%), microalbuminuria (473 patients, 25.4%),

metabolic syndrome (998 patients, 53.6%) and diabetes mellitus (544 patients, 29.2%). Of the 1862 patients with the high- or very high-risk factors, 1528 patients (82.1%) had more than and two high-risk factors. The distribution of the patients according to the ESH/ESC risk stratification is demonstrated in Table 1. Risk stratification has been substantially changed by the global risk evaluation (Figure 1). The percentages of patients defined as low, moderate and high-risk group by their providers (preevaluation) were 42, 44 and 14% compared with postevaluation percentages of 13, 27 and 60% using the ESH/ESC risk-assessment tool. A total of 1936 patients (62%) were reclassified to a higher and 219 (7%) to a lower risk category with systematic evaluation.

Comparison among the different risk groups according to the ESH/ESC risk stratification showed that the high-risk patients were older and had a male predominance, high BMI, longer duration of hypertension and low HDL-cholesterol (Table 2).

Table 3 Analysis of factors related to risk reclassification in Korean hypertensive patients

Variables	Estimate	s.e.	Odds ratio	95% CI		P-value
				Lower	Upper	
Age (years), Continuous variable	0.0243	0.0041	1.025	1.016	1.033	<0.0001
Gender, 1 = man, 0 = female	0.0493	0.0791	1.051	0.900	1.227	0.5330
BMI(kg m ⁻²), Continuous variable	-0.0472	0.0141	0.954	0.928	0.981	0.0008
SBP (mm Hg), Continuous variable	0.0235	0.0035	1.024	1.017	1.031	<0.0001
DBP (mm Hg), Continuous variable	0.0219	0.0054	1.022	1.011	1.033	<0.0001
Metabolic syndrome, 1 = Yes, 0 = No	0.2937	0.0889	1.341	1.127	1.597	0.0009
LVH, 1 = Yes, 0 = No	0.5096	0.2151	1.665	1.092	2.537	0.0178
CKD, 1 = Yes, 0 = No	0.3224	0.1024	1.380	1.129	1.687	0.0016
Microalbuminuria, 1 = Yes, 0 = No	-0.0404	0.1021	0.960	0.786	1.173	0.6923

Abbreviations: BMI, body mass index; CKD, chronic kidney disease; DBP, diastolic blood pressure; LVH, left ventricular hypertrophy; SBP, systolic blood pressure. CKD: yes (eGFR <60 ml min⁻¹ per 1.73 m²) calculated by Modification of Diet in Renal Disease equation. Microalbuminuria: yes (albumin-creatinine ratio Male: ≥ 22 mg g⁻¹, Female: ≥ 31 mg g⁻¹).

The BP control rate (target BP <140/90 mm Hg) was significantly lower in the high-risk group (72.1% in high-risk group compared with 97.5 and 97.3% in the low- and moderate-risk groups, respectively, $P < 0.0001$). The systolic and diastolic BPs were also significantly higher in the high-risk group. However, the use of combination therapy was more common in the low-risk group.

The global risk evaluation and adjustment of risk stratification had a significant impact on the evaluation of hypertension control. When we applied the recommended target goal of BP in patients with diabetes mellitus and CKD, the proportion of patients considered to be controlled was substantially changed in the low-to-moderate-risk patients, but not in the high-risk patients (Figure 2). In addition, the participating physicians considered that the BP of 2557 patients (82.2%) had been controlled before conducting an additional study; however, the global risk evaluation revealed that the BP of only 2030 patients (65.3%) had been controlled.

In the multiple logistic regression analysis, age, BMI, BP, metabolic syndrome, LVH and CKD were the independent factors associated with risk reclassification with global risk evaluation (Table 3).

DISCUSSION

Our survey yielded important observations regarding the risk profiles and the effect of global risk evaluation on the risk stratification in hypertensive patients treated by primary care physicians in Korea. (1) A total of 1862 patients (59.9%) had been classified to the high- or the very high-risk group in hypertensive patients treated by primary care physicians. (2) Simple tests evaluating organ damage such as ECG-LVH, microalbuminuria and estimated GFR had a substantial effect on the reclassification of the risk stratification, and subsequently on the control rate of hypertension. (3) Age, BMI, BP, metabolic syndrome, LVH and CKD were the determinant independent factors associated with the change of risk stratification. These are novel findings that will have impacts on the evaluation and management of Korean hypertensive patients.

Global risk assessment and management have been highlighted as the most frequently requested method to identify the high-risk group and to provide an optimal treatment plan for patients with hypertension.⁹ Accordingly, international treatment guidelines have recognized the importance of having multiple cardiovascular risk factors and have now begun to incorporate the concept of global cardiovascular risk evaluation and management to improve patient

outcomes, with a recommendation of global risk assessment in all hypertensive patients.

However, it is not clear how often the strategy is executed in real practice. Furthermore, specific examinations such as carotid ultrasound, echocardiography and pulse wave velocity require a special device or expert for the study. Accordingly, they have not been commonly performed by primary care physicians. In other words, it is impractical to execute them from the viewpoint of primary care physicians.

However, a simple blood test for the lipid panel, estimated GFR, electrocardiography and urinary albumin excretion may give additional information regarding the accompanying cardiovascular risk factors and TOD. There might be a substantial difference in the assessment of the risk profile in the hypertensive patients even after the simple essential test. Routine tests for risk factors and TOD may provide details on the hypertensive patients; however, how realistic such a strategy is in a primary care setting has not been shown.

In this study, most of the hypertensive patients treated by primary care physicians belonged to the high- or the very high-risk group. Previous studies also showed that the majority of the hypertensive patients treated by primary care physicians had high or very high-risk factors.¹⁰⁻¹² Moreover, we observed that the risk evaluation by primary care physicians was substantially changed as a result of additional simple tests. Because the physicians were not aware of the presence of risk factors and TOD in their daily practice, we thought that the main reason of misclassification was 'not obtaining data required for risk assessment'. Especially the physician reported that only 56 patients (1.8%) had CKD; however, the actual prevalence of CKD was 43.4% (1323 patients) in the study population.

Furthermore, it is possible that the reason of misclassification of the patients' risk was associated with poor interpretation of the basic laboratory results. In other words, although the primary care physician checked serum creatinine in their daily practice, the physician would not be aware the presence of CKD if he did not calculate estimated GFR with serum creatinine. In addition, if the physician did not check triglyceride, HDL-cholesterol and abdominal circumference regularly, he could not know whether the patients had metabolic syndrome or not.

In addition, we found that the majority of study population in the low- to moderate-risk group was reclassified; however, only 18.1% of the high-risk patients were reclassified with the additional test. Accordingly, the benefit of risk evaluation and stratification was

greatest in the moderate-risk group. These results are consistent with previous studies that showed the advantage of adding the evaluation of a simple organ damage marker to the risk charts in cardiovascular risk prediction, especially in the moderate group.^{13,14}

Incomplete risk evaluation has been associated with the use of antihypertensive treatment, which has not been considered as an indicator of the risk profile of the patients. In other words, more aggressive treatment was provided to the low-risk group; however, the BP was higher and combination therapy was less commonly used in the high-risk group.

When we compared the antihypertensive medication status according to the 'perceived risk', there was no significant difference among the low-, moderate- and high-risk groups (Appendix Table 1). However, the BP was higher and combination therapy was less commonly used in the 'estimated high-risk' group.

Furthermore, among the patients who were treated with combination therapy, 42.4, 38.9 and 36.0% of them used diuretics combination therapy in low, moderate and high-risk group, respectively ($P=0.04$). Accordingly, one of the reasons associated with poor rate of BP control might be lack of diuretics usage, especially in the high-risk group.

Accordingly, the discrepancy between patients' risk and antihypertensive treatment was derived from the gap between the 'perceived risk' by the primary care physician and the 'estimated risk' by the additional tests.

After risk stratification, the hypertension control rate was changed in the low-to-moderate-risk group, but there was no difference shown in the high-risk group. These data suggested that current hypertension treatment was provided irrespective of the risk in hypertensive patients.

When we analyzing the factors associated with reclassification, CKD (estimated GFR <60 ml min⁻¹ per 1.73 m²), LVH measured by ECG and metabolic syndrome, which can be identified with the additional tests, are the most significant factors associated with risk reclassification. A previous study also showed that the estimated GFR is significantly associated with fine tuning of the risk stratification.¹⁵ Interestingly, BMI had a negative impact on the reclassification of a risk group. In other words, physicians regarded obese hypertensive patients as the higher risk group; however, obese patients without metabolic syndrome or other TOD were reclassified into the lower-risk group. This result also implies that physicians tend to estimate the risk of hypertensive patients based on an impression, which leads to a substantial gap between the 'perceived risk' and the 'actual cardiometabolic risk' of the patients.

This survey was a cross-sectional study, which had several limitations regarding the generalizability of the conclusion. In addition, we did not perform specific examinations for the TOD, such as carotid IMT, echocardiography and pulse wave velocity. However, such tests need special devices and experiences for the proper evaluation. Therefore, such tests cannot readily be performed by primary care physicians. Accordingly, the tests evaluated in this study reflect the current situation in a primary care setting. Other countries, where specific tests are frequently performed for the hypertensive patients may show different results.

In addition, there are some methodological limitations in our study. We did not use a mercury sphygmomanometer for the measurement of BP because it is not easy to evaluate the appropriateness of BP measurement with a mercury sphygmomanometer in a nation-wide, epidemiological survey. Accordingly, any bias associated with electronic sphygmomanometer could have an influence on the data. However, the potential variability or unnecessary error

during BP measurements could be reduced by using an electronic sphygmomanometer.

In addition, the low prevalence of LVH in our data might be associated with the low sensitivity of ECG in detecting LVH. Finally, measurement of microalbuminuria at one time point is a limitation for the proper evaluation of renal damage, considering the day-to-day variability in the spot urine albumin/creatinine ratio.

In conclusion, the majority of hypertensive patients treated by primary care physicians belonged to the high- or the very high-risk group. In addition, even simple additional tests enhanced the risk evaluation of hypertensive patients. In other words, there was a substantial gap between the 'perceived risk' by the primary care physician and the 'estimated risk' by the global risk assessment. Accordingly, comprehensive cardiovascular risk stratification should be undertaken in all hypertensive patients. Furthermore, it is important to identify a strategy for improving the evaluation of organ damage by the primary care physician.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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APPENDIX

Demographic and laboratory characteristics according to the primary care physician's perceived risk stratification

	Low risk (N = 1312)	Moderate risk (N = 1365)	High risk (N = 432)	P-value
Age (years)	61.1 ± 11.4	62.8 ± 10.9	64.6 ± 11.5	<0.0001
Male gender, n (%)	546 (41.6)	703 (51.5)	253 (58.6)	<0.0001
BMI (kg m ⁻²)	24.7 ± 3.0	25.3 ± 3.1	25.8 ± 3.8	<0.0001
Waist circumference (cm)	87.1 ± 8.9	89.1 ± 8.5	91.3 ± 9.6	<0.0001
Current smoker, n (%)	159 (12.1)	290 (21.3)	111 (25.7)	<0.0001
Family history of HT	634 (48.3)	660 (48.4)	224 (51.9)	0.3988
Duration of HT (years)	5.3 ± 5.3	6.1 ± 5.9	6.7 ± 5.6	<0.0001
SBP (mm Hg)	129.0 ± 14.4	133.0 ± 14.6	136.7 ± 17.8	<0.0001
DBP (mm Hg)	78.9 ± 9.6	79.8 ± 9.6	80.1 ± 12.0	0.0057
LVH, n (%)	44 (3.4)	65 (4.8)	22 (5.1)	0.1196
Diabetes mellitus, n (%)	167 (12.7)	367 (26.9)	229 (53.0)	<0.0001
Glucose (mg dl ⁻¹)	103.0 ± 31.1	108.2 ± 37.0	117.7 ± 48.3	<0.0001
Hemoglobin A1c (%)	6.0 ± 0.8	6.2 ± 1.0	6.6 ± 1.1	<0.0001
Cholesterol, Total (mg dl ⁻¹)	186.4 ± 35.5	182.3 ± 36.7	176.1 ± 36.2	<0.0001
HDL-cholesterol (mg dl ⁻¹)	47.5 ± 12.1	46.4 ± 12.3	45.2 ± 11.6	0.0002
LDL-cholesterol (mg dl ⁻¹)	107.8 ± 32.5	104.6 ± 32.4	101.1 ± 32.7	<0.0001
Triglyceride (mg dl ⁻¹)	161.2 ± 99.2	169.1 ± 112.3	161.2 ± 92.0	0.4405
BUN (mg dl ⁻¹)	16.2 ± 4.7	16.4 ± 5.3	17.3 ± 6.6	0.0006
Creatinine (mg dl ⁻¹)	1.0 ± 0.2	1.0 ± 0.3	1.1 ± 0.4	<0.0001
Urine microalbumin (µg ml ⁻¹)	28.3 ± 87.0	34.5 ± 112.3	62.4 ± 145.8	<0.0001
Urine protein (mg dl ⁻¹)	13.1 ± 21.1	22.8 ± 211.8	23.0 ± 62.1	0.0930
Urine creatinine (mg dl ⁻¹)	115.8 ± 73.4	120.9 ± 76.8	115.2 ± 75.2	0.5837
<i>Anti-HT medication, n (%)</i>				
ACEI/ARB	206 (15.9)	241 (17.9)	68 (16.0)	0.3571
Beta-blocker	55 (4.3)	37 (2.7)	17 (4.0)	
Calcium channel blocker	189 (14.6)	187 (13.9)	67 (15.8)	
Diuretic	4 (0.3)	9 (0.7)	2 (0.5)	
Combination therapy	838 (64.9)	876 (64.9)	271 (63.8)	

Abbreviations: ACEI/ARB, angiotensin converting enzyme inhibitor/angiotensin II receptor blocker; BMI, body mass index; BUN, blood urea nitrogen; DBP, diastolic blood pressure; HDL, high-density lipoprotein; HT, hypertension; LDL, low-density lipoprotein; LVH, left ventricular hypertrophy; SBP, systolic blood pressure.