Original Article

Characteristics of Young-Onset White Coat Hypertension Identified by Targeted Screening for Hypertension at a University Health Check-Up

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Previously we estimated the prevalence of essential hypertension (EH) as around 0.1% and suggested that male gender, obesity, and strong genetic background (hypertension in parents) were risk factors for EH in a young population aged less than 30 based on targeted screening for hypertension at a university health check-up. This study also revealed a high incidence of white coat hypertension (WCH) in university students, and thus, we continued this screening for four consecutive years, and examined the prognosis and clinical characteristics of young-onset WCH. Three occasions of casual blood pressure (BP) measurement and additional home BP measurement revealed 72 WCH and 15 EH students (all males) during the 4-year study period. None of the WCH students had elevated home BP to the level of hypertension during their stay at university, and 26 out of 38 WCH students participating screening in the following years showed normal casual BP. Although WCH students showed a significantly higher pulse rate than controls, WCH could not be fully differentiated from EH either by pulse rate or by correlation between casual BP value and pulse rate. These findings indicate the requirement of longer follow-up after graduation to determine the prognosis of young-onset WCH, though EH and WCH in the young population share the same risk factors and, possibly, autonomic nervous system dysfunction. Since diagnosis of WCH has limited importance for university students, screening of EH following a general health check-up would elevate the clinical validity of casual BP measurement at the university. (*Hypertens Res* 2008; 31: 1063–1068)

***Key Words*: young-onset hypertension, essential hypertension, home blood pressure measurement**

Introduction

Blood pressure (BP) measurement is routinely performed at the general health check-up in most universities and colleges in Japan. We previously introduced a targeted-screening system for hypertension at Tohoku University, which required the students with a high casual BP at regular check-up to return for BP measurements as well as to make their own BP measurements at home (home BP), until the diagnosis of each student was determined (*1*). This screening system suggested that the prevalence of hypertension (all essential hypertension [EH]) requiring medication was around 0.1% in the young population aged less than 30, and demonstrated that male gen-

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Table 1. Results of Targeted Screening for Hypertension for Consecutive 4 Years

	School year			
	2003	2004	2005	2006
Total students (30 or younger)	16,464	17,032	16,376	16,493
↓				
1st screening	12,563 (76.3)	12,303 (72.2)	12,288 (75.0)	11,114 (67.4)
Hypertensive students	1,354	1,367	1,649	1,311
↓				
2nd screening	789 (58.3)	937 (68.5)	1,085 (65.8)	936 (71.4)
Hypertensive students	78	80	99	105
↓				
3rd screening	55 (70.5)	57 (71.3)	70 (70.7)	79 (75.2)
Hypertensive students	22	29	33	22
↓				
Home BP measurement	22 (100)	26 (89.6)	32 (97.7)	20 (90.9)
Normal limit (WCH)	16	23	27	17
Hypertensive students (further examination at university hospital)	6	3	5	3
↓				
Diagnosis of hypertension				
Essential hypertension (EH)	6 (100)	3 (100)	3 (60)	3 (100)
Secondary hypertension	0	0	0	0

WCH, white coat hypertension. Numbers in parenthesis mean consultation rate (%).

der, obesity and a strong genetic background for hypertension (hypertension in their parents) are risk factors for young onset EH (*1*). Since home BP measurement was included in our screening process, we also noted a higher prevalence of white coat hypertension (WCH) in young subjects. Although WCH in the general population is considered a pre-condition of EH (*2–4*), the clinical characteristics and prognosis of young-onset WCH remain to be elucidated. Therefore, we asked the WCH students to receive regular check-ups in the following years without observation bias, and examined the prognosis of these WCH students during their stay at university.

In addition to the diagnosis of WCH, several studies, including our previous study (*1*, *5*, *6*), have reported a high incidence of WCH in the young population. At first casual BP measurement at a general health check-up, more than 10% of university students aged less than 30 demonstrated a BP of 140/90 mmHg or higher (*1*). Although we used this casual BP measurement as an initial step for the systematic screening of hypertension, no standardized clinical procedures for hypertensive students at a university general check-up have been determined. The number of hypertensive students at a general check-up is too large to ask all hypertensive students to visit the hospital, and our previous study suggested that the students requiring medical treatment for hypertension are far fewer than the hypertensive students at the first casual BP measurement (*1*). Therefore, the clinical requirements following casual BP measurement should be evaluated to establish the clinical validity of casual BP measurement at the university general health check-up. To this end, we examined the prognosis and clinical parameters of WCH students to investigate the clinical characteristics of young-onset WCH. We then discussed the validity of casual BP measurement at the university health check-up based on the clinical characteristics of WCH in university students.

Methods

All students (around 18,000 students in each year) of Tohoku University were asked to undergo a regular health check-up, including a BP measurement (1st BP) at Tohoku University Health Center. The BP was measured under the supervision of well-trained nurses using an automatic device (BP-203RVII; Nippon Colin Co., Ltd., Komaki, Japan) on the right upper arm with the subject in a sitting position after resting for at least 5 min. Repeated BP measurement was not performed for the hypertensive subjects, since additional arrangements were made for the BP measurement of these subjects. About a month later, we re-measured the BP of students with a systolic BP of 140 mmHg or greater and/or a diastolic BP of 90 mmHg or greater (2nd BP). The students who again showed a high BP (based on the threshold values defined above) were asked to undergo a third BP measurement, which was performed by a doctor together with a questionnaire administration after a more than 30-min rest (3rd BP). The doctor then checked the familial history of hypertension and selected students with the same regimen mentioned above, who were

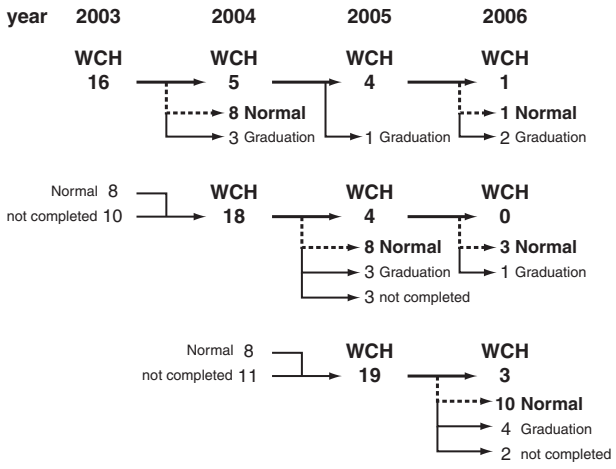

Fig. 1. *Diagnostic alteration of white coat hypertension (WCH) from 2003 to 2006.*

asked to measure their BP at home (home BP), in the morning, using a fully automated, digital display device (HEM 747IC; Omron Life Science, Kyoto, Japan) that they were given by the health center. According to the guidelines of the Japanese Society of Hypertension, the first measurement in the morning was recorded for more than 2 weeks, and the mean of the BP values and pulse rates on different mornings (more than 7 measurements) was calculated and used as the home BP (home BP). Finally, the students with a systolic home BP of 135 mmHg or greater and/or a diastolic home BP of 85 mmHg or greater were referred to the Tohoku University Hospital for a detailed examination. The results of students aged less than 30 years old were analyzed. The students showing home BP of less than 135/85 mmHg were diagnosed as having WCH. These WCH students were asked to receive regular health check-ups the following year. The study protocol was approved by the Institutional Review Board of Tohoku University School of Medicine and performed over the Japanese school year from 2003 to 2006.

Our previous study on EH and WCH students revealed a high prevalence of strong genetic back ground (hypertension in their parents) (*1*), and we noticed that the genetic information of hypertensive relatives other than their parents was incorrect in many students aged less than 30. Therefore, we prepared a separate questionnaire directly asking about the presence or absence of hypertension in their father and/or mother and administered it along with the regular questionnaires at the general health check-up in 2006.

The differences between data were examined for statistical significance using an unpaired *t*-test followed by the Student's *t*-test. The results are expressed as the means±SD. A p value <0.05 was considered statistically significant.

Table 2. Clinical Parameters of Students with Consistent or Transient WCH

Variables	Consistent WCH	Transient WCH
Number	12	26
Age (years)	20.8±2.0	21.8±1.7
Casual BP		
Systolic (mmHg)	158.8±13.3	149.7±10.5
Diastolic (mmHg)	90.6±7.5	84.7±9.0
Pulse (bpm)	103.3±26.0	90.6±12.8
Home BP		
Systolic (mmHg)	122.8±5.6	121.9±7.3
Diastolic (mmHg)	76.8±5.3	73.1±6.6
Pulse (bpm)	60.8±8.9	62.4±7.6
BMI	25.0±3.7	24.0±4.4
EH in parents (%)	5 (42)	14 (54)

BP, blood pressure; EH, essential hypertension; WCH, white coat hypertension; BMI, body mass index. Data are mean±SD.

Results

The numbers of students who underwent each step of BP measurement during four consecutive school years are demonstrated in Table 1. In every year, two occasions (1st and 2nd measurement) of casual BP measurement markedly reduced the number of hypertensive subjects, and the third BP measurement by medical doctors further decreased the number of hypertensive students to around 30, as we reported previously (*1*). All of the hypertensive students who were required to measure home BP were males. Although we did not show the number of females at each step in the present study, the results for females in 2005 and 2006 were quite similar to those in 2003 and 2004, which were demonstrated in our previous study (*1*). The percentage of attendance at each step was also similar in every year. The final numbers of students requiring medical treatment for hypertension were less than ten students in each year. Seventeen students in total showed high BP even at home, and 15 of them visited the university hospital and were diagnosed as having EH. The majority of students showing high BP at three occasions of casual BP measurement demonstrated normal BP values at home. Because twelve students were diagnosed as having WCH again in the following years, the total number of students with WCH was 72.

Since WCH students were asked to receive a regular check-up for the following years, 38 WCH students completed the targeted screening for hypertension for more than two consecutive years (Fig. 1). Twenty-six out of 38 WCH students demonstrated a normal BP value at casual BP measurement in the next year (transient WCH), and 12 of them demonstrated high BP values at three occasions of casual BP measurement, and were required to measure home BP again (consistent WCH). However, their home BP values remained almost unchanged,

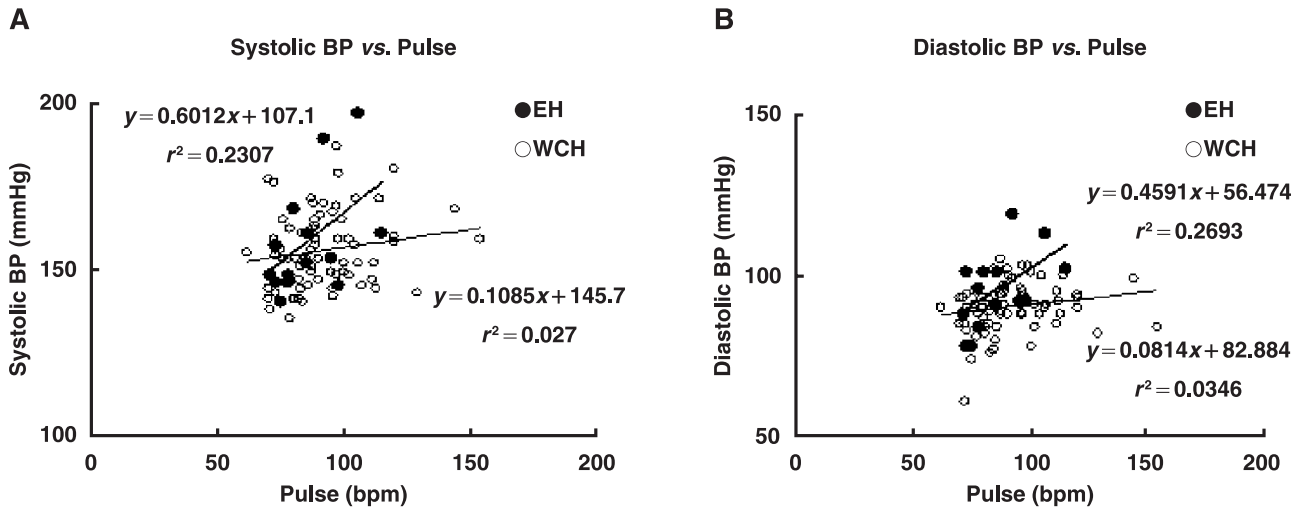

Fig. 2. *Correlation between blood pressure (BP) values and pulse rate at 1st BP in essential hypertension (EH) and white coat hypertension (WCH) students. A: Between systolic BP value and pulse rate. B: Between diastolic BP value and pulse rate.*

and none of them were diagnosed as having EH (Fig. 1). Although we examined the clinical values of consistent WCH at general check-up by comparing them with those of transient WCH (Table 2), there were no significant differences in these values except for a slightly higher prevalence of strong genetic back ground in consistent WCH. Even in the 7 WCH students who were diagnosed with WCH during the consecutive 2 or 3 years, 4 students demonstrated a normal casual BP value in the following year (Fig. 1).

Clinical parameters at general check-up, such as age, gender, BP values of 1st casual BP measurement, pulse rate, body mass index (BMI), and percentage presence of strong genetic background (EH in parents) in EH, WCH, and male students receiving regular check-up in 2006 (controls) are shown in Table 2. Casual BP values, both systolic BP and diastolic BP, and BMI of EH and WCH students were significantly higher than those of controls. There were no significant differences in these parameters between EH and WCH students. The percentage presence of a strong background for hypertension was markedly higher in EH students than in controls. This score was also much higher in WCH students than in controls, though it was slightly lower than that in EH students. The pulse rate of WCH students was significantly increased when compared to that of controls. The pulse rate of EH students tended to be increased, and there was no significant difference in pulse rate between EH and WCH students. Table 2 also shows the home BP values and pulse rate at home of EH and WCH students. Although the pulse rates of both EH and WCH students were normalized at home, the home BP values of EH students were significantly higher than those of WCH students. Most of the EH or WCH students were non-smokers, as we reported previously (*1*).

Since the pulse rate of WCH students was significantly increased and that of EH students tended to be increased, we examined the correlation between BP values and pulse rate at 1st BP measurement in these students (Fig. 2). Both systolic (Fig. 2A) and diastolic (Fig. 2B) BP values of EH students tended to be correlated with pulse rate, whereas such correlations with pulse rate were almost completely absent in WCH students (Fig. 2). Therefore, most of the students showing a systolic BP less than 150 mmHg and pulse rate more than 90 bpm were WCH students, and all students with diastolic BP less than 90 mmHg and pulse rate more than 90 bpm were WCH students. However, students with a systolic BP 150 mmHg and more and/or diastolic BP of 90 mmHg and more could be either EH or WCH.

Discussion

Three occasions of casual BP measurements resulted in similar number of hypertensive students for further evaluation, as we described in our previous study (*1*), and additional home BP measurement revealed more WCH students than EH students. As our system asked WCH students to receive regular check-ups and subsequent steps of targeted screening without observation bias, we previously found two types of WCH students: a group of WCH students who demonstrated normal casual BP in the next year (transient WCH), and another group of WCH students who again showed a high casual BP and normal home BP (consistent WCH) (*1*). The clinical parameters of consistent WCH were more close to those of EH students when compared to those of transient WCH (*1*). Thus, we presumed that some of the consistent WCH students would show development of EH during their stay at the university. Since 4 years is the standard period for most university students in Japan, we presently continued the targeted-screening system for 4 consecutive years. The results demonstrated that none of the constant WCH students elevated their

Table 3. BP, Pulse, BMI and Genetic Background of Students

Variables	EH	WCH	Male students in 2006
Number	15	72	8,102
Age (years)	21.4±2.35	21.7±2.36	21.5±2.6
Casual BP			
Systolic (mmHg)	158.6±16.3*	155.7±11.4*	125.7±14.3
Diastolic (mmHg)	95.8±11.6*	90.4±7.6*	73.8±12.1
Pulse (bpm)	85.7±13.1	92.0±17.3*	78.4±18.4
Home BP			
Systolic (mmHg)	142.7±8.7#	122.6±8.0	
Diastolic (mmHg)	89.3±9.6#	74.5±6.3	
Pulse (bpm)	65.5±6.5	62.2±7.2	
BMI (kg/m^2)	26.4±4.2*	24.9±4.0*	21.8±3.5
HT in parents (*n*/total (%))	13/15 (86.7)	38/72 (52.7)	722/7,123 (10.1)

BP, blood pressure; EH, essential hypertension; WCH, white coat hypertension; BMI, body mass index; HT, hypertension. Data are mean±SD. *$p<0.05$ *vs*. data of male students in 2006 and #$p<0.05$ *vs*. data of WCH.

home BP to the level of EH. On the contrary, one of the constant WCH students diagnosed in 2003 showed a normal casual BP in 2006. Although the follow-up period was shorter for WCH students diagnosed in 2004, such normalization of casual BP was noted in all constant WCH students. These findings suggest that the follow-up period of young-onset WCH requires a much longer period after the graduation to determine prognosis. In addition, as Frontini and coworkers reported that awareness of hypertension highly influenced the attitude toward medical care in a young population (*7*), awareness of normal BP at home might influence the following of casual BP measurement in WCH students. Diagnosis of WCH, then, may have limited clinical importance for university students aged less than 30, at least during the period of their stay at the university.

Our present study included a greater number of students with both consistent and transient WCH than our previous study (*1*), and thus we compared the clinical parameters of these two types of WCH again (Table 3). The results demonstrated the absence of a significant difference between consistent WCH and transient WCH. Up to one-third of WCH students did not complete the targeted screening for the next year mainly due to their graduation, and therefore the numbers of students for both consistent WCH ($n=12$) and transient WCH ($n=26$) were not sufficient for the statistical analysis. Thus, the relatively low follow-up rate of WCH students would be an additional study limitation, along with the short follow-up period at the university, limiting the full determination of the characteristics and prognosis of young-onset WCH. These results, however, may also suggest the limited clinical importance of a diagnosis of consistent WCH at the university health check-up.

As we failed to show the clinical significance of the diagnosis of consistent WCH, we examined the clinical parameters of WCH without separating WCH into constant and transient WCH. In our previous study, we noticed that most university students had incorrect clinical information on their family history for hypertension, and only the information on their parents was clear. We then prepared an extra questionnaire asking about hypertension in their fathers and/or mothers at a general health check-up in 2006. In addition, all WCH and EH students diagnosed in the present study were males. Therefore, the clinical parameters of male students in 2006 were used as a control in the present study. Our previous study presented the casual BP values and BMI of male and female students in 2003 and 2004, and we confirmed that these values of male students in 2006 were almost the same as those in male students in 2003 and 2004. As we reported in our previous study (*1*), significantly higher BMI was noted in both EH and WCH students than in controls, and there was no significant difference between EH and WCH students. Then, a novel finding was the markedly higher prevalence of a strong genetic background in both EH and WCH students than in controls. Although a recall bias due to the direct questionnaire by medical doctors might have increased the number of students with a strong genetic background in EH and WCH students, such a large difference strongly suggested the presence of a genetic background for hypertension in these students. These findings suggest that EH and WCH students share the same risk factors, such as male gender, higher BMI, and high prevalence of a strong genetic background. Sharabi *et al*. reported the influence of obesity on BP in young adults (*8*), and Kavey *et al*. recently examined the BP response to exaggerated exercise and cardiac function of WCH children and suggested that WCH in children would be a pre-hypertensive state (*9*). Our present finding also suggests the close association between EH and WCH in young subjects. Thus, WCH students, at least some of them, would develop EH later in their life. Such development, however, seldom occurs during the period of university enrollment, as mentioned above.

The pulse rate at the general health check-up was significantly increased in WCH students when compared to that in

control male subjects, and thus, we examined the correlation between BP values and pulse rate in both WCH and EH students. The results demonstrated the absence of correlation in WCH students, while EH students demonstrated a weak correlation. These findings suggested that most students with a low grade elevation (systolic BP from 140 to 150 mmHg) and/or normal range diastolic BP (less than 90 mmHg) of casual BP were WCH students, if their pulse rate was more than 90 bpm. However, we could not differentiate WCH from EH in students with higher casual BP values (systolic BP more than150 mmHg and/or diastolic BP more than 90 mmHg). Therefore, home BP measurement in addition to casual BP measurements is considered an indispensable way to screen EH students. Several previous reports have indicated the sympathetic nerve dominant dysfunction in the autonomic nerves in EH (*10–12*), and Neumann and coworkers have demonstrated the same pattern of autonomic nervous system dysfunction in WCH subjects (*13*). Although we did not perform a detailed examination of the autonomic nerve system, the difficulty in separating EH and WCH by pulse rate or pulse rate–related parameters might support the previous finding that EH and WCH share the same type of autonomic nervous system dysfunction (*13*).

Our present study revealed the requirement of long follow-up for a full determination of the clinical characteristics of young onset WCH, though young-onset EH and young-onset WCH share some clinical risk factors. The lack of WCH students developing EH while attending the university also suggests that screening of EH might be more important clinically than the diagnosis of WCH for university students aged less than 30. Therefore, a screening system for hypertension performed after casual BP measurement at a general health check-up would elevate the clinical validity of casual BP measurement at the university.

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