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ORIGINAL ARTICLE

Home blood pressure level and decline in renal function among treated hypertensive patients: the J-HOME-Morning Study

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We examined the association between home and office blood pressure (BP) levels and further decline in renal function among treated hypertensive patients with and without renal dysfunction. We calculated annual decline in estimated glomerular filtration rate (ΔeGFR) in 1535 treated hypertensive patients with home and office BP measurements. We defined ΔeGFR <0 as decline in renal function, and ΔeGFR $\geqslant 0$ as non-decline in renal function based on 1.5 years of follow-up. For 520 patients with low eGFR at baseline, morning home, evening home and office systolic BP (SBP) levels and morning home diastolic BP (DBP) levels were positively associated with the risk of decline in renal function (trend $P=0.003$, 0.002, 0.003 and 0.004). Compared to patients with home SBP <125 mm Hg, the risk of decline in renal function was higher in those with home SBPs $\geqslant 135$ mm Hg and between 130–135 mm Hg, while the risk was similar in those with home SBP of 125–130 mm Hg. For 1015 patients with normal eGFR at baseline, only morning home SBP level was positively associated with the risk of decline in renal function (trend $P=0.004$). Morning home BP might be useful for risk evaluation of decline in renal function even among treated hypertensive patients with normal renal function. Target levels of home BP control among treated hypertensive patients need to be further investigated.

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Keywords: decline in renal function; estimated glomerular filtration rate; home blood pressure; treated hypertensive patients

INTRODUCTION

Chronic kidney disease (CKD) is currently a major public health problem. In Japan, it is reported that patients with CKD comprise approximately 13% of the adult population.[1] CKD is a risk factor for end-stage renal disease,[2–4] stroke[5–7] and death.[8,9] Hypertension is one of the risk factors for the development of CKD. Control of home and office systolic blood pressure (SBP) has been found to be closely associated with renal function among patients with CKD.[10–13] In other words, adequate control of SBP might be important for the improvement of renal and cardiovascular prognosis among patients with CKD.

The Japanese Society of Hypertension Guidelines for the Management of Hypertension 2014 (JSH2014) recommend a target office SBP of <130 mm Hg and home SBP of <125 mm Hg among hypertensive patients with CKD.[14] The target office SBP level among patients with CKD was established based on evidence from many studies.[15–17] However, evidence for the target home SBP among CKD patients is limited, even though many studies have demonstrated that home BP is superior to office BP in many respects.[18] The recommended target home SBP level is not based on sufficient evidence and is provisional; it was merely calculated based on the criterion that in hypertensives, the home SBP value (135 mm Hg among patients without CKD and 125 mm Hg among patients with CKD) should be 5 mm Hg lower than that of the office SBP value (130 and 140 mm Hg, respectively, for patients with and without CKD).[14]

The aim of the present study was to assess the association between home and office BP levels and further decline in renal function among treated hypertensive patients with and without kidney dysfunction.

METHODS

Patients

We examined data from patients who had enrolled in the Japan Home versus Office Blood Pressure Measurement Evaluation (J-HOME)-Morning Study, which investigated the influence of appropriate control of home BP on the

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progression of vascular complications among treated hypertensive patients in Japan. The details of the methods used in this study have been described previously.[19] In October 2004, 3994 randomly selected physicians from across Japan were invited to participate in the J-HOME-Morning Study. Of the 957 physicians who agreed to participate, 398 collected data for the study. Patients were eligible to participate in the present study if they met the following criteria: (1) ⩾20 years of age; (2) diagnosed as having essential hypertension; (3) treated with antihypertensive drugs; (4) measurements of morning home BP, evening home BP and office BP were available; and (5) provided written informed consent to participate in this study. Physicians could enroll all patients who met the inclusion criteria regardless of gender and BP levels. By the end of June 2006, 2497 patients who provided written informed consent for study participation were enrolled. We excluded 38 patients with insufficient data on BP values or other characteristics, and 14 who were not being treated with antihypertensive drugs. Therefore, 2445 patients were eligible for the J-HOME-Morning Study. After 1.5 years from baseline survey, we followed up on only 2086 of these patients since serum creatinine values (Scr), which were used for calculating the estimated glomerular filtration rate (eGFR), were missing in 359 patients who were, therefore, excluded. Of the 2086 patients, 246 were lost to follow-up, 85 had insufficient data on BP values or major parameters at follow-up, and 220 had insufficient data on follow-up Scr values in the second survey. Therefore, this study population comprised 1535 patients. Among the 2445 initially eligible patients, the excluded patients ($n=910$) were significantly older, with a greater proportion of alcohol consumption and family history of hypertension than the patients ultimately included in the study. The home and office BP levels were significantly higher among the excluded patients than in those included. The Institutional Review Board of Tohoku University School of Medicine approved the study protocol.

Evaluation of renal function

We calculated eGFR as the index of renal function. The formula used to calculate eGFR was the Japanese equation for GFR estimation:[20]

$$\mathrm{eGFR}\left(\mathrm{ml\ min^{-1}\ per 1.73 m^2}\right) = 194 \times \mathrm{Scr}^{-1.094} \times \mathrm{age}^{-0.287} (\times 0.739 \text{ if female}).$$

Scr was determined by the enzymatic method.

We additionally calculated the annual reduction of eGFR (ΔeGFR) as:

$$\Delta\mathrm{eGFR}\left(\mathrm{ml\ min^{-1}\ per 1.73 m^2\ per year}\right) = (\text{follow} - \text{up eGFR} - \text{baseline eGFR})/\text{follow} - \text{up period}.$$

Then, we defined 'decline in renal function' as ΔeGFR <0 and 'non-decline in renal function' as ΔeGFR $\geqslant 0$ ml min^{-1} per 1.73 m^2 per year.

Measurement of home BP

The patients used the following procedures specified in the Japanese guidelines for home BP measurements.[18] They measured their own BP, while seated, once every morning for 2 weeks within 1 h of waking and after at least 2 min of rest but before ingesting medications and breakfast, and once every evening immediately before bedtime by cuff-oscillometry using electronic arm-cuff devices. The Ministry of Health, Labour and Welfare of Japan has validated and approved all such devices that are presently available in the country.[21] The actual models were not described by the physicians who participated in the study, but all devices for measuring BP were certified as having been adjusted to the Association for the Advancement of Medical Instrumentation standards.[21,22] The means of all measurements recorded over the 2-week period was calculated for each patient and subsequently analyzed.

Measurement of office BP

The BP values of the patients were consecutively measured twice while seated and after resting for 1–2 min during regular attendance at the participating institutions. Physicians (63.4%) or nurses (36.6%) used the auscultation method with a mercury (50.3%) or aneroid (4.9%) sphygmomanometer, or the cuff-oscillometric method with electronic arm-cuff devices (44.8%). The mean of four measurements at two clinic visits during the period of home measurements was defined as the office BP value for each patient and was included in the analysis.

Data collection and statistical analysis

Information about the patients' characteristics and antihypertensive medication was collected from a questionnaire administered by the attending physician at the time of patient recruitment. We examined the association between decline in renal function and BP level at baseline. We calculated the odds ratio (OR) for decline in renal function (ΔeGFR <0 ml min^{-1} per 1.73 m^2 per year) in each home BP category (125–130, 130–135 and ⩾135 mm Hg for home SBP, and 75–80, 80–85 and ⩾85 mm Hg for home diastolic BP (DBP)), as compared with a home SBP of <125 mm Hg or home DBP of <75 mm Hg, respectively. We also calculated the OR for decline in renal function in each office BP category (130–135, 135–140 and ⩾140 mm Hg for office SBP, and 80–85, 85–90 and ⩾90 mm Hg for office DBP), compared with an office SBP of <130 mm Hg or office DBP of <80 mm Hg, respectively. These classifications were based on JSH2014, which recommended defining home SBP/DBP $<125/75$ mm Hg and office SBP/DBP $<130/80$ mm Hg as normal home BP and normal office BP, respectively; and home SBP/DBP ⩾135/85 mm Hg and office SBP/DBP ⩾140/90 mm Hg as hypertension for home BP and office BP, respectively. These analyses were performed in two groups: patients with normal eGFR (⩾60 ml min^{-1} per 1.73 m^2), and patients with low

Table 1 Baseline characteristics of the study population

	Normal eGFR at baseline (⩾ *60 ml min^{-1} per 1.73 m^2*) n = *1015*	*Low eGFR at baseline* (< *60 ml min^{-1} per 1.73 m^2*) n = *520*
Age, year	65.7 ± 10.7	71.1 ± 9.4
Men, %	46.8	43.9
Body mass index, kg m^{-2}	24.1 ± 3.4	24.1 ± 3.2
Current smoker, %	10.1	11.2
Current drinker, %	25.3	24.6
Family history of hypertension, %	42.3	47.5
Complications		
History of stroke, %	7.4	9.8
History of ischemic heart disease, %	6.2	12.5
Diabetes, %	15.9	21.4
Dyslipidemia, %	51.2	55.4
High uric acid, %	15.3	29.2
Baseline eGFR, ml min^{-1} per 1.73 m^2	75.9 ± 12.9	49.1 ± 8.1
Follow-up eGFR, ml min^{-1} per 1.73 m^2	74.8 ± 14.3	47.1 ± 8.0
ΔeGFR, ml min^{-1} per 1.73 m^2 per year	-0.6 ± 9.2	5.2 ± 8.8
Treat period ⩾1 year, %	51.0	59.2
Number of drugs ⩾3, %	24.3	39.2
Class of drug, %		
Ca channel blockers	73.1	79.2
ARBs	56.2	58.1
ACE inhibitors	13.6	15.4
Diuretics	14.3	22.5
β-blockers	13.4	21.5
α-blockers	16.0	15.8
αβ-blockers	6.0	7.9

Abbreviations: ACE, angiotensin-converting enzyme; ARBs, angiotensin II receptor blockers; eGFR, estimated glomerular filtration rate.

eGFR (<60 ml min^{-1} per 1.73 m^2).[14] Data are expressed as means ± s.d. Variables were compared using Student's *t*-test, the χ^2-test or multivariate logistic regression analysis, as appropriate. The multivariate model was adjusted for variables that were significantly associated in the bivariate analysis. For multiple comparison, the Bonferroni correction was applied and $P<0.002$ was considered significant. All data were statistically analyzed using SAS software, version 9.3 (SAS Institute, Cary, NC, USA).

RESULTS

Among the 1015 patients with normal eGFR, the mean age was 65.7 ± 10.7 years, 46.8% were men and the mean eGFR at baseline was 75.9 ± 12.9 ml min^{-1} per 1.73 m^2 (Table 1). Among the 520 patients with low eGFR, the mean age was 71.1 ± 9.4 years, 43.9% were men and the mean eGFR at baseline was 49.1 ± 8.1 ml min^{-1} per 1.73 m^2.

Among the 1015 patients with normal eGFR at baseline, baseline eGFR was significantly higher in patients with a decline in renal function compared with those with non-decline in renal function ($P<0.002$) (Table 2). The proportions of patients with a family history of hypertension, receiving ⩾3 antihypertensive drugs, receiving Ca channel blockers, and receiving αβ-blockers, were significantly different between the patients with and without decline in renal function ($P<0.05$).

The ORs for decline in renal function among the BP categories are shown in Figures 1 and 2. For the 1015 patients with normal eGFR at baseline, the risk for decline in renal function was significantly higher in those with morning home SBP ⩾135 mm Hg than in patients with morning home SBP <125 mm Hg, and there was no association between morning home, evening home and office DBP categories and decline in renal function.

In the 520 patients with low eGFR at baseline, the risk of decline in renal function was significantly higher among those with morning home SBP ⩾135 mm Hg and those with morning home DBP ⩾85 mm Hg than among patients with morning home SBP <125 mm Hg and those with morning home DBP <75 mm Hg. The risk was higher in patients with a morning home SBP of 130–135 mm Hg and those with a morning home DBP of 80–85 mm Hg than in those with a morning home SBP of 125–130 mm Hg (OR = 1.82, 95% confidence interval = 0.95–3.45) and those with a morning home DBP of 75–80 mm Hg (OR = 2.35, 95% confidence interval = 1.29–4.28), respectively. The risk was significantly higher in patients with an evening home SBP ⩾135 mm Hg than in patients with an evening home SBP <125 mm Hg. The risk was higher in patients with an evening home SBP of 130–135 mm Hg and those with evening home DBP of 80–85 mm Hg than those with an evening home SBP of 125–130 mm Hg (OR = 2.04, 95% confidence interval = 1.05–3.97) and those with an evening home DBP of 75–80 mm Hg (OR = 2.12, 95% confidence interval = 1.05–4.27), respectively. The risk of decline in renal function was significantly higher among patients with SBP

Table 2 Comparison of patients' characteristics in terms of non-decline and decline in kidney function between patients with normal and low eGFR at baseline

	Normal eGFR at baseline (n = *1015*)		*Low eGFR at baseline* (n = *520*)	
Change of renal function (ΔeGFR)	*Non-decline (⩾0)*	*Decline (<0)*	*Non-decline (⩾ 0)*	*Decline (<0)*
Number of patients	254	761	310	210
Age, year	64.5 ± 12.0	66.1 ± 10.2	69.8 ± 9.8	73.1 ± 8.5**
Men, %	48.4	46.3	43.9	43.8
Body mass index, kg m^{-2}	24.1 ± 3.6	24.1 ± 3.3	24.1 ± 3.3	24.0 ± 3.0
Current smoker, %	9.1	10.4	12.3	9.5
Current drinker, %	29.1	24.1	28.7	18.6*
Family history of hypertension, %	48.0	40.3*	53.2	39.1**
Complications				
History of stroke, %	7.9	5.7	7.1	13.8*
History of ischemic heart disease, %	7.9	7.2	11.0	14.8
Diabetes, %	14.6	16.3	21.3	21.4
Dyslipidemia, %	49.2	51.9	58.1	51.9
High uric acid, %	35.8	30.5	46.1	56.2*
Baseline eGFR, ml min^{-1} per 1.73 m^2	70.5 ± 10.0	77.7 ± 13.3**	49.5 ± 7.4	48.5 ± 9.0
Follow-up eGFR, ml min^{-1} per 1.73 m^2	85.1 ± 14.7	71.3 ± 12.4**	63.3 ± 11.6	45.2 ± 10.3**
ΔeGFR, ml min^{-1} per 1.73 m^2 per year	10.6 ± 7.0	-4.4 ± 6.5**	10.2 ± 7.9	-2.2 ± 2.8**
Treat period ⩾1 year, %	52.8	50.5	62.6	54.3
Number of drugs ⩾3, %	29.1	22.7*	40.3	37.6
Class of drugs, %				
Ca channel blockers	78.4	71.4*	81.0	76.7
ARBs	52.8	57.3	53.9	64.3*
ACE inhibitors	13.0	13.8	14.2	17.1
Diuretics	15.8	13.8	21.6	23.8
β-blockers	15.8	12.6	24.8	16.7*
α-blockers	17.3	15.5	15.2	16.7
αβ-blockers	8.7	5.1*	7.4	8.6

Abbreviations: ACE, angiotensin-converting enzyme; ARBs, angiotensin II receptor blockers; eGFR, estimated glomerular filtration rate.
*$P<0.05$; **$P<0.002$ vs non-decline in each group. $P<0.002$ was considered significant based on the Bonferroni correction.

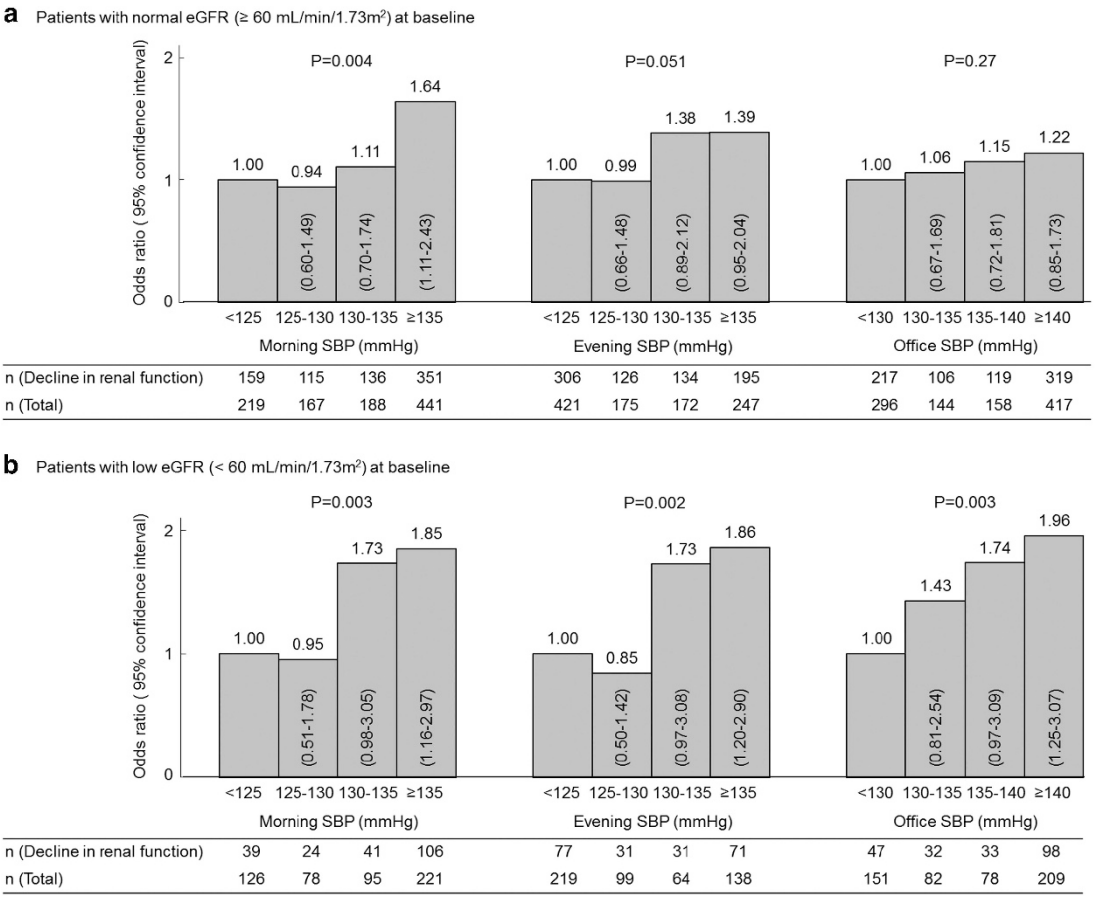

Figure 1 Association between morning home, evening home and office SBPs and the risk of decline in renal function. The model among patients with normal eGFR (⩾60 ml min^{-1} per 1.73 m^2) at baseline was adjusted for baseline eGFR. The model among patients with low eGFR (<60 ml min^{-1} per 1.73 m^2) at baseline was adjusted for age and family history of hypertension. The *P*-level for linear trend is indicated above the bars. The numbers inside the bars indicate 95% confidence intervals. The lowest BP category was treated as the reference category. eGFR, estimated glomerular filtration rate; SBP, systolic blood pressure.

⩾140 mm Hg and those with an office DBP of 85–90 mm Hg than that in patients with an office SBP <130 mm Hg and those with an office DBP <75 mm Hg.

DISCUSSION

In the present study, the risk of decline in renal function increased in patients with home SBP ⩾130 mm Hg as compared with patients with home SBP <130 mm Hg in patients with baseline eGFR <60 ml min^{-1} per 1.73 m^2 (Figure 1). These results might suggest the importance of controlling home SBP to at least below 130 mm Hg in treated hypertensive patients with decreased renal function. Morning home SBP in patients with normal renal function and morning home DBP in patients with decreased renal function were linearly associated with decline in renal function, whereas evening home and office BPs were not.

In the group of patients with low eGFR at baseline, the risk of decline in renal function among patients with home SBP ⩾130 mm Hg was higher than among patients with home SBP <130 mm Hg. Okada *et al.*[12] found that the annual decline in eGFR was significantly greater among patients with morning home SBP ⩾130 mm Hg than among those with morning home SBP <130 mm Hg in patients with CKD. Agarwal *et al.*[23] reported that the cumulative risk of end-stage renal disease among subjects with home SBP ⩾130 mm Hg was significantly higher than that among subjects with morning home SBP <130 mm Hg, this being independent of office BP control. However, Okada *et al.*[24] also reported that the risk of progression of CKD did not differ between patients with morning home SBP <125 mm Hg and patients with morning home SBP ⩾125 mm Hg. Therefore, from the perspective of preventing a decline in renal function, the evidence to indicate whether control of home SBP below 125 mm Hg might be superior to control of morning home SBP to below 130 mm Hg is scarce. These results were broadly consistent with the results of the Hypertension Objective Treatment Based on Measurement by Electrical Devices of Blood Pressure (HOMED-BP) Study. The HOMED-BP Study demonstrated that, in patients with essential hypertension, the 5-year risk for poor cardiovascular outcomes was minimal if home SBP of patients under treatment was ⩽131.6 mm Hg.[25]

JSH2014 has recommended an office SBP of <130 mm Hg as the target value among hypertensive patients with CKD.[14] In the present study, among patients with a low eGFR, although office SBP also showed a significant linear relationship with the risk of decline in renal function, we could not find the cut-off value of office SBP to distinguish the risk. Bakris *et al.* reported in a systematic review that progression of renal dysfunction was prevented by maintaining office SBP at <130 mm Hg.[17] Thus, the results of the present study would partially support the results of previous studies.

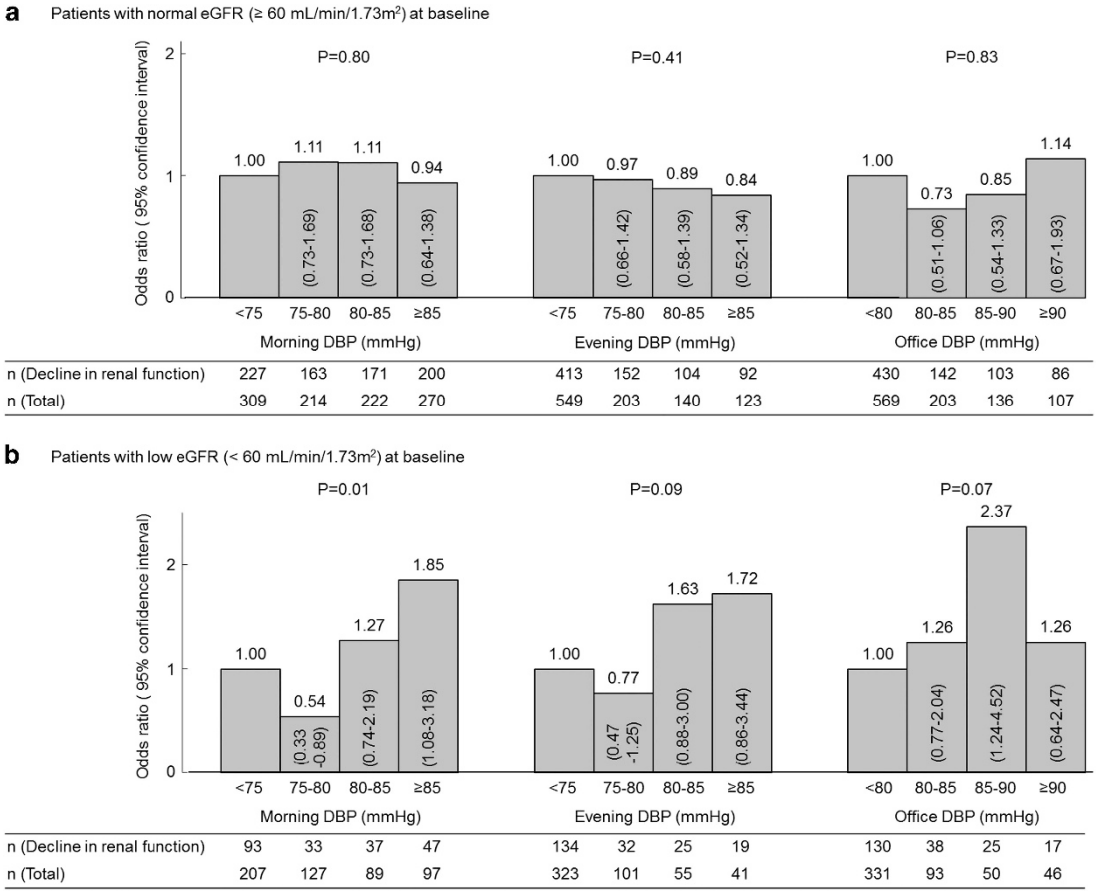

Figure 2 Association between morning home, evening home and office DBPs and the risk of decline in renal function. The model among patients with normal eGFR ($\geq$60 ml min^{-1} per 1.73 m^2) at baseline was adjusted for baseline eGFR. The model among patients with low eGFR ($<$60 ml min^{-1} per 1.73 m^2) at baseline was adjusted for age and family history of hypertension. The *P*-level for linear trend is indicated above the bars. The numbers inside the bars indicate 95% confidence intervals. The lowest BP category was treated as the reference category. DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate.

In the present study, among patients with a low eGFR at baseline, all the morning home, evening home and office SBP levels were associated with a decline in renal function. However, among patients with normal eGFR at baseline, only morning home SBP was associated with a decline in renal function. These results are consistent with the results of the Ohasama Study, which found that home BP was useful for risk stratification of patients with a lower stage of hypertension.[26] Therefore, morning home BP might be useful for evaluation of the risk of decline in renal function even among treated hypertensive patients with normal renal function.

This study has certain limitations. First, our study is limited in the reliability and reproducibility of evaluation of renal function, because the Scr values used for calculating eGFR at baseline and during follow-up were based on only one measurement of Scr each, and the institutions that measured Scr varied among the study subjects. Second, we could not assess whether the patients had proteinuria. Recently, it was reported that intensive BP control (office SBP/DBP $<$130/80 mm Hg) was effective in the preservation of renal function only in patients with proteinuria.[27] Further studies are required that would consider not only eGFR, but also other indices of renal function, such as proteinuria. The other limitations of the present study are that we could not obtain data on the subjects' BP values before starting antihypertensive treatment. In addition, this study was not an interventional study, but rather, an observational study. Therefore, further research is needed to establish appropriate target BP levels for home BP. In this study, a single home measurement was taken on each occasion. Current Japanese guidelines recommend duplicate self-home measurements to be performed.[14] Thus, home BP levels have probably been overestimated in this study. However, we found that even a single measurement of home BP was helpful for the risk evaluation of treated hypertensive patients.

In conclusion, elevated morning home, evening home and office SBPs, and morning home DBP levels were positively associated with the risk of decline in renal function in treated hypertensive patients with eGFR $<$60 ml min^{-1} per 1.73 m^2; the risk of decline in renal function in patients with home SBP $\geqslant$ 130 mm Hg was higher than that in patients with home SBP $<$130 mm Hg. In treated hypertensive patients with eGFR $\geqslant$60 ml min^{-1} per 1.73 m^2, on the other hand, only morning home SBP level was positively associated with the risk of decline in renal function. Therefore, morning home BP might be useful for evaluation of the risk of decline in renal function even among treated hypertensive patients with normal renal function. Target levels of home and office BP control need to be investigated further.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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The names of all the participating practitioners have been previously published.[19]

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