# Routine Use of Ambulatory Blood Pressure Monitoring in Potential Living Kidney Donors

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**Background and Objectives: Most transplant centers exclude prospective living kidney donors with hypertension from donation. Centers routinely identify hypertension using BP measured in the clinic, but it is not clear that clinic BP accurately detects the presence or absence of hypertension in potential donors. We therefore conducted a prospective study to determine the impact of routine ambulatory BP monitoring on diagnosis of hypertension in potential donors and the value of other baseline characteristics in predicting ambulatory BP results.**

**Design, Setting, Participants, & Measurements: We compared classification of hypertension status by clinic BP and by ambulatory BP monitoring in 178 potential living kidney donors.**

**Results: Of 63 individuals with hypertension by clinic BP, 62% had white-coat hypertension by ambulatory BP and were therefore eligible to donate. Of 115 individuals who were normotensive by clinic BP, 17% had masked hypertension by ambulatory BP and were excluded from donation. Individuals with masked hypertension were older, were more likely to be male, and had a somewhat higher clinic BP than individuals with sustained normotension. Individuals with white-coat hypertension had a somewhat lower clinic diastolic BP than individuals with sustained hypertension.**

**Conclusions: Routine ambulatory BP monitoring may identify a large number of individuals with white-coat hypertension and a smaller but significant number of individuals with masked hypertension, ensuring adequate protection of potential donors and accurate assessment of donor risk. Differences in baseline characteristics are small and are not clinically useful in distinguishing individuals with masked hypertension from individuals with sustained normotension or individuals with white-coat hypertension from individuals with sustained hypertension, demonstrating the importance of ambulatory BP monitoring in this population.**

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Living kidney donation is becoming increasingly more important in renal transplantation. The number of living donors has doubled in the past 10 yr, whereas the number of cadaveric donors has remained relatively stagnant (1). Meanwhile, the size of the kidney transplantation waiting list has continued to grow, and the number of deaths among patients who are awaiting transplant continues to increase (1). This has prompted transplant centers to reevaluate their eligibility criteria for prospective living donors. The majority of transplant centers exclude potential donors with hypertension from donating because of concerns that nephrectomy may increase the long-term medical risks of hypertension after donation (2), and in fact hypertension is the most common medical reason for exclusion from donation (3–5). Clinic BP measurement is the most common method of identifying hypertension. It is not clear, however, that BP measured in the transplant clinic accurately detects the presence or absence of hypertension in potential donors.

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Ambulatory BP monitoring measures BP many times during the course of a 24-h day in a patient's usual setting. Numerous studies have shown that ambulatory BP is more closely associated with target-organ damage than clinic BP and is a better predictor of cardiovascular events and death than clinic BP (6–10). Ambulatory BP monitoring can also identify white-coat hypertension, when BP is elevated in clinic but normal on ambulatory monitoring, and masked hypertension, when BP is normal in clinic but elevated on ambulatory monitoring. Large population studies have shown that individuals with white-coat hypertension have less target-organ damage than those with sustained hypertension and rates of cardiovascular events similar to those with sustained normotension (11–14). Conversely, individuals with masked hypertension have rates of target-organ damage and cardiovascular events similar to those with sustained hypertension (11–14). The routine use of ambulatory BP monitoring in the evaluation of potential living kidney donors may identify patients with white-coat and masked hypertension, thereby ensuring appropriate identification of true hypertension status and accurate assessment of donor risk.

## Materials and Methods

The study protocol was approved by our institutional review board, and all participants provided written informed consent. Potential living kidney donors who underwent physician evaluation at the Transplan-



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tation Institute of the Mount Sinai Medical Center during a 30-mo period from 2004 to 2006 were invited to participate. All potential donors underwent blood-group testing and initial evaluation by a transplant nurse coordinator before being referred for physician evaluation by a transplant nephrologist. Any donor who was ABO-incompatible with their intended recipient or who had a personal history of a donor exclusion criterion, including hypertension, did not proceed to the physician evaluation and was not eligible to participate in this study.

BP was obtained on two occasions by clinic staff during quiet sitting using an automated oscillometric device (Welch Allyn, Skaneateles Falls, NY), and the mean of these measurements was recorded as the clinic BP. Ambulatory BP was obtained using automated Spacelabs 90217 ambulatory BP monitors (Spacelabs Medical, Issaquah, WA), which measured BP every 20 min during the day and every 30 min at night. Correlation readings were performed at the time of monitor placement using a sphygmomanometer, and those with a >5-mmHg difference between the sphygmomanometer BP and monitor BP were excluded. Also excluded were individuals with an arm circumference of >42 cm or fewer than 10 awake and 4 asleep ambulatory BP readings. Awake and asleep times were determined by patient self-report.

Hypertension by clinic BP was defined in accordance with the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure guidelines as ≥140/90, and hypertension by ambulatory BP was defined according to American Society of Hypertension guidelines as a mean 24-h ambulatory BP ≥130/80. Participants were categorized as having (*1*) sustained normotension (normotensive by clinic and ambulatory BP), (*2*) white-coat hypertension (hypertensive by clinic BP but normotensive by ambulatory BP), (*3*) masked hypertension (normotensive by clinic BP but hypertensive by ambulatory BP), or (*4*) sustained hypertension (hypertensive by clinic and ambulatory BP).

Baseline characteristics were compared between groups that had the same diagnosis of normotension or hypertension by clinic BP; that is, between individuals with sustained normotension and individuals with masked hypertension and between individuals with white-coat hypertension and individuals with sustained hypertension. Parameters of ambulatory BP were compared between groups that had the same diagnosis of normotension or hypertension by ambulatory BP monitoring; that is, between individuals with sustained normotension and individuals with white-coat hypertension and between individuals with masked hypertension and individuals with sustained hypertension. Analyses were performed using Intercooled Stata 8.2 software (Stata Corp., College Station, TX). Comparisons of continuous variables were performed using the independent-sample *t* test, and comparisons of categorical variables were performed using the Pearson $\chi^2$ test. All tests were two-tailed, and $\alpha$ was set at 0.05.

## Results

A total of 203 of the 249 potential living donors evaluated at our center during the study period consented to participate in the study. Twenty-five (12%) of these were excluded, all for an inadequate number of ambulatory BP readings, leaving 178 participants in the study. Characteristics of included participants, excluded individuals, and all potential donors evaluated during the study period are shown in Table 1. Of note, >30% of individuals were black, and >30% were Hispanic, which reflects the diverse racial and ethnic mix of our patient population.

The relationship of clinic and ambulatory BP for each individual is illustrated in Figure 1. There was a modest and statistically significant positive correlation between BP values for both systolic (SBP) and diastolic BP (DBP; $r = 0.56$ [$P < 0.001$] and $r = 0.66$ [$P < 0.001$], respectively). Categorization of participants as hypertensive by clinic or ambulatory BP is shown in a 2 × 2 format in Table 2. Of 63 participants who were classified as hypertensive by clinic BP, 62% were normotensive by ambulatory BP and were identified as having white-coat hypertension. Of 115 participants who were classified as normotensive by clinic BP, 17% were hypertensive by ambulatory BP and were identified as having masked hypertension. Using ambulatory BP as the gold standard, clinic BP misdiagnosed 33% of the 178 participants. The number of potential donors identified as normotensive increased by 11% with the use of ambulatory BP monitoring in this study sample.

*Table 1.* Baseline characteristics of potential donors[a]

| Characteristic | All Potential Donors ($n = 249$) | Study Participants | |
|---|---|---|---|
| | | Included ($n = 178$) | Excluded ($n = 25$) |
| Age | 40 ± 12 | 41 ± 11 | 40 ± 7 |
| Gender | | | |
| male | 96 (39) | 71 (40) | 9 (36) |
| female | 153 (61) | 107 (60) | 16 (64) |
| Race[b] | | | |
| white | 135 (54) | 108 (61) | 15 (60) |
| black | 56 (22) | 56 (31) | 9 (36) |
| other | 22 (9) | 14 (8) | 1 (4) |
| Ethnicity[b] | | | |
| Hispanic | 66 (27) | 54 (30) | 9 (36) |
| non-Hispanic | 172 (69) | 124 (70) | 16 (64) |

[a]Data are means ± SD or *n* (%).
[b]Race and ethnicity information not available for all potential donors.

Baseline characteristics of participants are listed in Table 3 according to their hypertension grouping. Participants with masked hypertension were somewhat older (44 *versus* 37 yr), were more likely to be male (70 *versus* 40%), and had a higher clinic SBP and DBP (128 *versus* 119 and 81 *versus* 75 mmHg, respectively) compared with participants with sustained normotension. Participants with sustained hypertension had a greater clinic DBP than those with white-coat hypertension (92 *versus* 88 mmHg) but were otherwise similar.

Figure 2 illustrates the range of clinic BP values within groups and compares those groups that have a statistically significant difference in mean values. All individual SBP and DBP values in the masked hypertension group are within the range of values in the sustained normotension group. With the exception of one outlier, all individual clinic DBP values in the sustained hypertension group are within the range seen in the white-coat hypertension group.

Table 4 shows the parameters of ambulatory BP according to participants' hypertension grouping. Participants with white-coat hypertension had a significantly higher ambulatory BP than those with sustained normotension (117 *versus* 113 and 73

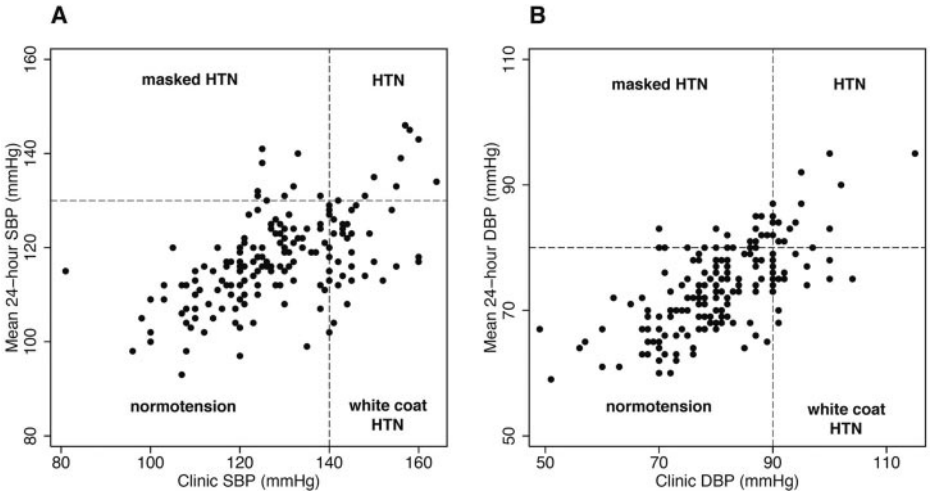


*Figure 1.* Clinic BP *versus* 24-h ambulatory BP for systolic BP (SBP; A) and diastolic BP (DBP; B). Dashed lines are drawn at threshold values of BP.

*versus* 70 mmHg for 24-h BP; 122 *versus* 117 and 77 *versus* 74 mmHg for awake BP; 107 *versus* 103 and 64 *versus* 62 mmHg for asleep BP). Participants with sustained hypertension had a significantly higher awake DBP than those with masked hypertension (88 *versus* 84 mmHg), but ambulatory BP parameters were otherwise similar between the two groups. The degree of nocturnal dip in BP was similar in individuals with white-coat hypertension compared with individuals with sustained normotension and in individuals with sustained hypertension compared with individuals with masked hypertension.

## Discussion

There are very few data regarding the impact of elevated BP on long-term outcomes of living donors, largely because most transplant centers consider hypertension to be an exclusion criterion for donation. Several studies have found that hypertension before donation may be associated with worsened control of BP after donation (15–17), and one study reported that donors with higher levels of clinic BP before donation had a greater decline in renal function after donation (17). The only prospective study to evaluate outcomes in donors with hypertension found that the decline in iothalamate GFR was similar at 11 mo after donation in donors with normotension and hypertension. Because most of the donors with hypertension were treated with an angiotensin receptor blocker, the effect of donation on BP and proteinuria in these individuals is unclear (18). Given the current body of knowledge, most centers continue to be wary of accepting donors with hypertension. It is therefore essential that the diagnosis of hypertension be made using the best available method.

*Table 2.* Absence or presence of hypertension by clinic or ambulatory BP[a]

| Clinic BP Hypertension | Ambulatory BP Hypertension | | Total |
|---|---|---|---|
| | Present | Absent | |
| Present | 24 (13.4%) | 39 (21.9%) | 63 (35.4%) |
| Absent | 20 (11.2%) | 95 (53.4%) | 115 (64.6%) |
| Total | 44 (24.7%) | 134 (75.3%) | 178 |

[a]Clinic BP hypertension defined as ≥140/90; ambulatory BP hypertension defined as mean 24-h ≥130/80.

Ambulatory BP has been shown in multiple studies to be a better predictor of target organ damage and of outcomes than clinic BP (6–10). Individuals with white-coat hypertension have less target-organ damage and fewer cardiovascular events than individuals with sustained hypertension (12,13,19,20), whereas individuals with masked hypertension have rates of target-organ damage and cardiovascular risk similar to those in individuals with sustained hypertension (12,13,21). Using ambulatory BP monitoring, we identified a large number of potential donors who were incorrectly classified as having hypertension by clinic BP but actually had white-coat hypertension. We also identified a smaller but important group of potential donors who had masked hypertension and had been incorrectly classified as having normotension by clinic BP. Through this study, we were able to assess more accurately the medical risk for potential donors and at the same time increase the pool of eligible donors at our center.

This study is the first to attempt to identify baseline characteristics that may aid in discriminating potential donors with masked hypertension from those with sustained normotension and potential donors with sustained hypertension from those with white-coat hypertension. Although clinic SBP and DBP were significantly higher in the masked hypertension group than in the sustained normotension group, there was a great deal of overlap in individual values between groups, making clinic BP unlikely to be helpful in distinguishing true hypertension status. Similarly, although clinic DBP was significantly higher in the sustained hypertension group compared with the white-coat hypertension group, the actual difference between groups was smaller than the SD around the means and not clinically useful in distinguishing the two groups. Individuals

*Table 3.* Baseline characteristics by group[a]

| Characteristic | Sustained Normotension ($n = 95$) | Masked Hypertension ($n = 20$) | White-Coat Hypertension ($n = 39$) | Sustained Hypertension ($n = 24$) |
|---|---|---|---|---|
| Age | 37 ± 11 | 44 ± 10[e] | 44 ± 12 | 45 ± 12 |
| Male gender | 38 (40) | 14 (70)[e] | 13 (33) | 6 (25) |
| Black race | 32 (33) | 6 (30) | 9 (23) | 9 (38) |
| Hispanic ethnicity | 38 (40) | 6 (30) | 7 (18) | 3 (13) |
| First-degree relative of recipient | 50 (53) | 7 (35) | 18 (46) | 10 (42) |
| Family history of hypertension | 67 (71) | 16 (80) | 28 (72) | 20 (83) |
| BMI | 27 ± 5 | 29 ± 4 | 28 ± 5 | 27 ± 4 |
| Clinic SBP (mmHg) | 119 ± 11 | 128 ± 6[f] | 142 ± 9 | 145 ± 11 |
| Clinic DBP (mmHg) | 75 ± 8 | 81 ± 6[f] | 88 ± 8 | 92 ± 8[g] |
| Serum creatinine (mg/dl) | 0.8 ± 0.2 | 0.9 ± 0.2[e] | 0.8 ± 0.1 | 0.8 ± 0.2 |
| Creatinine clearance (ml/min)[b] | 129.1 ± 32.8 | 131.1 ± 22.1 | 115.3 ± 26.7 | 114.6 ± 21.3 |
| eGFR (ml/min per 1.73 $m^2$)[c] | 110 ± 24 | 100 ± 24 | 101 ± 20 | 105 ± 21 |
| Microalbuminuria[d] | 7 (7) | 2 (10) | 3 (8) | 2 (8) |

[a]Data are means ± SD or frequency (%). BMI, body mass index; DBP, diastolic BP; eGFR, estimated GFR; SBP, systolic BP.
[b]Calculated from 24-h urine collection.
[c]Calculated from simplified Modification of Diet in Renal Disease (MDRD) equation.
[d]Defined as urine microalbumin:creatinine ratio >30 mg/g.
[e]$P < 0.05$ for masked hypertension *versus* sustained normotension.
[f]$P < 0.005$ for masked hypertension *versus* sustained normotension.
[g]$P < 0.05$ for sustained hypertension *versus* white-coat hypertension.

with masked hypertension were older and more likely to be male than individuals with sustained normotension, but the relatively small age difference and that almost one third of individuals with masked hypertension were female prevent either of these characteristics from being helpful in the determination of true hypertension status.

Ambulatory BP parameters were higher in individuals with white-coat hypertension than in individuals with sustained normotension. The cardiovascular risk of ambulatory BP is, like that of clinic BP, continuous and without a clear lower threshold. This suggests that living donors with white-coat hypertension may be at a somewhat greater cardiovascular risk than those with sustained normotension. Whether this also suggests a greater renal risk in donors with white-coat hypertension is unknown. However, all parameters of ambulatory BP were similar in the masked hypertension group and the sustained hypertension group, with the exception of a slightly higher awake DBP in the individuals with sustained hypertension.

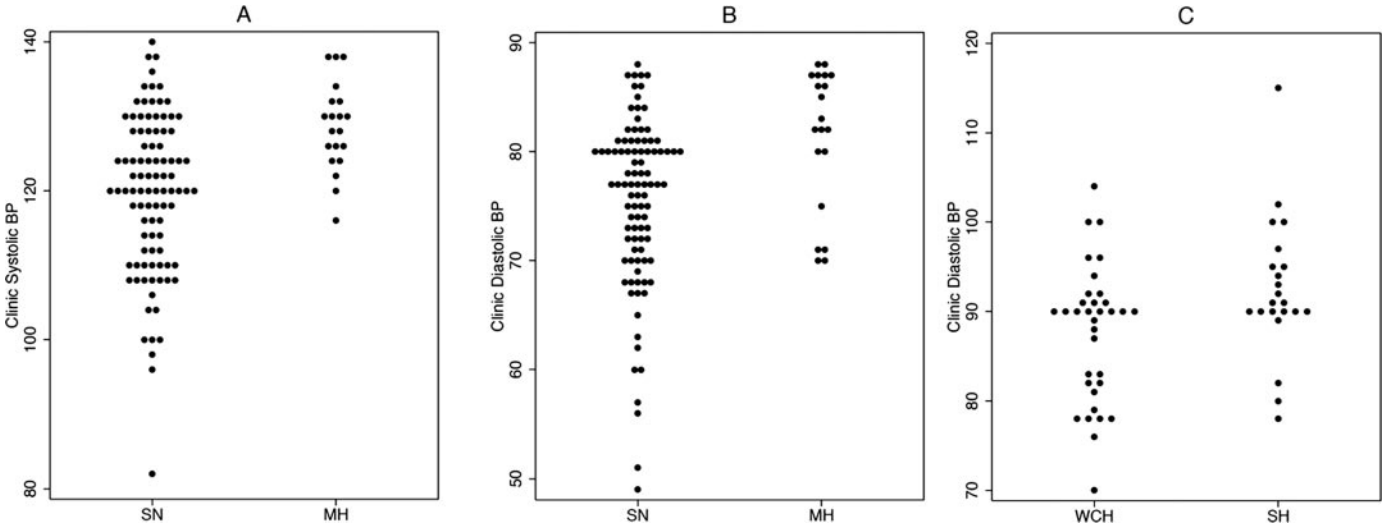


*Figure 2.* Range of clinic BP values for groups with statistically significant differences in mean values. (A) Clinic SBP for sustained normotension (SN) and masked hypertension (MH). (B) Clinic DBP for SN and MH. (C) Clinic DBP for white-coat hypertension (WCH) and sustained hypertension (SH).

*Table 4.* Ambulatory BP parameters by group[a]

| Parameter | Sustained Normotension ($n = 95$) | White-Coat Hypertension ($n = 39$) | Masked Hypertension ($n = 20$) | Sustained Hypertension ($n = 24$) |
|---|---|---|---|---|
| Mean 24-h | | | | |
| SBP | 113 ± 7 | 117 ± 6[c] | 128 ± 6 | 129 ± 8 |
| DBP | 70 ± 5 | 73 ± 4[c] | 81 ± 2 | 84 ± 5 |
| Awake | | | | |
| SBP | 117 ± 8 | 122 ± 6[c] | 133 ± 6 | 134 ± 9 |
| DBP | 74 ± 6 | 77 ± 6[c] | 84 ± 3 | 88 ± 5[e] |
| Asleep | | | | |
| SBP | 103 ± 8 | 107 ± 9[d] | 115 ± 10 | 117 ± 8 |
| DBP | 62 ± 6 | 64 ± 5[d] | 72 ± 8 | 73 ± 7 |
| Nocturnal dip[b] | 11.5 ± 5.5 | 12.8 ± 5.5 | 13.1 ± 5.8 | 12.6 ± 5.1 |

[a]Data are means ± SD.
[b]Defined as (awake SBP − asleep SBP)/awake SBP × 100%.
[c]$P < 0.05$ for white-coat hypertension *versus* sustained normotension.
[d]$P < 0.005$ for white-coat hypertension *versus* sustained normotension.
[e]$P < 0.05$ for sustained hypertension *versus* masked hypertension.

This suggests an identical cardiovascular and renal risk in living donors with masked hypertension and those with sustained hypertension.

Two groups previously reported on the routine use of ambulatory BP monitoring in potential living donors. Textor *et al.* (22), in a study from the Mayo Clinic in Minnesota, compared identification of hypertension by routine clinic BP with that by ambulatory BP or standardized office BP. Although the authors reported a rate of white-coat hypertension of 70% and a rate of masked hypertension of 3.5%, they considered individuals to be have normotension when either the ambulatory or the standardized office BP was within the normal range. There was in fact a high rate of disagreement between diagnosis of hypertension by ambulatory BP monitoring and by standardized office readings, leading to an overestimation of white-coat hypertension and an underestimation of masked hypertension in this study.

In a Turkish study of 126 potential donors with normotension or mild hypertension by clinic BP, 65% of individuals who had hypertension by clinic BP had white-coat hypertension, and 7% of individuals who were classified as having normotension by clinic BP had masked hypertension (23). Of note, all individuals with masked hypertension had target-organ damage on retinal examination and/or echocardiogram, whereas none of those with white-coat hypertension had evidence of target-organ damage. It is unclear why the rate of masked hypertension was lower in that study than in this study, although little information regarding baseline characteristics of participants was provided in that study.

This study is the first to report on the use of ambulatory BP monitoring in a racially and ethnically diverse group of potential donors, with 30% black and 30% Hispanic participants. The National Health and Nutrition Examination Survey has shown that black individuals have a higher prevalence of hypertension and Hispanic individuals have a lower prevalence of hypertension compared with non-Hispanic white individuals. How race or ethnicity may affect ambulatory BP has not been clearly established. One study that compared the relationship of race to white-coat effect did find that there was a greater white-coat effect in whites than in black individuals (24); no data are available on the impact of Hispanic ethnicity on ambulatory relative to clinic BP. In our study, however, we found no difference in race or ethnicity between individuals with sustained normotension and individuals with masked hypertension or between individuals with white-coat hypertension and individuals with sustained hypertension.

Routine ambulatory BP monitoring is an additional burden to potential donors and to transplant centers and an additional expense to the health care system. It is clear, however, that ambulatory BP monitoring in patients who are deemed to have hypertension by clinic BP will identify a large number of individuals with white-coat hypertension and therefore enable otherwise ineligible patients to proceed with donation. This benefits potential donors who are eager to donate, recipients who are otherwise faced with an extended wait before receiving a transplant, and a health care system that is overwhelmed by the high cost of care of a growing dialysis population. We believe that this study also shows that ambulatory BP monitoring should be performed on patients who have normotension in clinic as well as those who have hypertension. The prevalence of masked hypertension in this study is significant given that it occurs in otherwise healthy people who are ready to place themselves at risk to benefit others. Sensitivity of clinic BP in detecting hypertension in this study was only 44%. Given the increased rates of end-organ damage and cardiovascular events in individuals with masked hypertension, this group of potential donors must be identified so that the prospective donor and his or her transplant physician may better understand potential risks.

The recommendation for routine ambulatory BP monitoring

in potential donors requires an implicit assumption that white-coat hypertension does not increase medical risk in living donors. Although no study has shown a greater rate of cardiovascular events in individuals with white-coat hypertension, some data suggest that white-coat hypertension is not a benign phenomenon. Several studies have reported rates of target-organ damage greater than that in individuals with sustained normotension, although lower than those in individuals with sustained hypertension (11,13,25), whereas a large population study in Japan found that incidence of sustained hypertension at 10-yr follow-up was higher among individuals with white-coat hypertension than individuals with sustained normotension (26). In this study, ambulatory BP was higher in the white-coat hypertension group than in the sustained normotension group. The sum of the data suggests that it will likely be safe to accept donors with white-coat hypertension but that they may benefit from increased surveillance after donation. Our data are part of a prospective study designed to follow long-term outcomes of living donors, including those with white-coat hypertension. Ambulatory BP monitoring offers great promise and possibility for living-donor kidney transplantation. However, as our eligibility criteria for living donors evolve, we must ensure careful study of the effects on donors, including long-term follow-up of donors who are accepted under these new standards.

The findings of this research must be interpreted with certain caveats. The participation rate of eligible donors in this study was 82%. Although demographic characteristics of included participants seem similar to those of all eligible donors, it is possible that included study participants are different from nonparticipants in ways that may affect the relationship between clinic BP and ambulatory BP. Finally, although we have shown that ambulatory BP is superior to clinic BP in determining hypertension status in potential living donors, the impact of hypertension or exclusion of donors with hypertension on living-donor outcomes is unknown. Assessing the impact of routine ambulatory BP in evaluating potential living donors will require long-term follow-up of medical outcomes after donation.

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## Disclosures

None.

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