

REVIEW PAPER

Current status of ambulatory blood pressure monitoring in Asian countries: A report from the HOPE Asia Network

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Abstract

Ambulatory blood pressure monitoring (ABPM) can measure 24-hour blood pressure (BP), including nocturnal BP and diurnal variations. This feature of ABPM could be of value in Asian populations for preventing cardiovascular events. However, no study

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has yet investigated regarding the use of ABPM in actual clinical settings in Asian countries/regions. In this study, 11 experts from 11 countries/regions were asked to answer questionnaires regarding the use of ABPM. We found that its use was very limited in primary care settings and almost exclusively available in referral settings. The indications of ABPM in actual clinical settings were largely similar to those of home BP monitoring (HBPM), that is, diagnosis of white-coat or masked hypertension and more accurate BP measurement for borderline clinic BP. Other interesting indications, such as nighttime BP patterns, including non-dipper BP, morning BP surge, and BP variability, were hardly adopted in daily clinical practice. The use of ABPM as treatment guidance for detecting treated but uncontrolled hypertension in the Asian countries/regions didn't seem to be common. The barrier to the use of ABPM was primarily its availability; in referral centers, patient reluctance owing to discomfort or sleep disturbance was the most frequent barrier. ABPM use was significantly more economical when it was reimbursed by public insurance. To facilitate ABPM use, more simplified indications and protocols to minimize discomfort should be sought. For the time being, HBPM could be a reasonable alternative.

1 | INTRODUCTION

Hypertension is one of the most important risk factors for cardiovascular events and mortalities.¹ The absolute burden of hypertension in Asian countries is rapidly increasing, especially in the recent 10 years; this is similar to the trends observed in sub-Saharan Africa.² Such burden is explained by the increasing prevalence of hypertension owing to Westernization, modernization, and urbanization, as well as insufficient blood pressure (BP) control. Thus, the incidence of uncontrolled hypertension has doubled in the last 30 years.³

Hypertension in Asians has unique features with higher mortality and morbidity in relation to stroke than to ischemic heart disease.⁴ And the correlation slope between BP and cardiovascular events in Asian populations is significantly steeper than that in Western populations.⁵ At the same time, BP control was demonstrated to be very effective in reducing the incidence of stroke in Asian populations.⁶⁻⁸

In these respects, there could be more interest in using ambulatory BP monitoring (ABPM) to assist in earlier diagnosis and thorough BP control. In fact, there is accumulating evidence that morning surge is more associated with cardiovascular outcomes in Asian populations than in Western populations; furthermore, nocturnal BP is known to be a more important factor in Asian populations because of higher salt intake and salt sensitivity and/or higher central BP.^{9,10} ABPM could be useful for demonstrating BP variabilities.¹¹ For these reasons, a consensus document from Asian experts was recently published, and more active adoption of ABPM in clinical practice is expected in the future.¹²

As the first step to facilitate the implementation of ABPM, the current use of ABPM and its feasibility and barriers in actual clinical practice in Asian countries/regions were investigated in this study.

2 | METHODS AND MATERIALS

2.1 | Recruitment of expert panels

We recruited 11 hypertension specialists who published at least one article related to ABPM from 11 countries/regions: China (C), India (I), Indonesia (In), Japan (J), Korea (K), Malaysia (M), Pakistan (Pa), Philippines (Ph), Singapore (S), Taiwan (Ta), and Thailand (Th) as expert panels.

2.2 | Questionnaire for the current status of ABPM

We employed a questionnaire to obtain information regarding the current use and protocol, availability of guidelines, availabilities, and cost of ABPM. The detailed questions are listed in Table 1. Regarding the measurement protocol, the measurement interval, definition of daytime and nighttime, criteria for erroneous reading, and minimum required readings were assessed. Regarding the clinical use of ABPM, the indication; diagnostic thresholds; definition of white-coat hypertension and masked hypertension; definition of non-dipper BP, extreme dipper BP, and morning surge; application of BP variability and nighttime BP patterns to practice; preference between ABPM and home BP monitoring (HBPM); ABPM as a treatment guidance; ABPM treatment target; and Asian perspective of ABPM were evaluated. Regarding the barriers, the availability of ABPM in primary care and referral settings, availability of measurement using 4-point Likert scales (>75%, 50%-75%, 25%-50%, and <25%), cost of a session of ABPM in US dollars (USDs), and reimbursement by public or private insurances were assessed.

All questionnaires were reviewed and summarized according to questions, with the corresponding countries/regions presented in abbreviations.

TABLE 1 Items in the questionnaires to ask the current use, guidelines or protocols, availability, and cost for ambulatory blood pressure monitoring in Asian countries

1. Are guidelines for using ABPM in your country?
2. Protocol for ABPM measurement
 1. What is the measurement interval during day and night?
 2. How to define daytime and nighttime?
 3. What is the exclusion criteria for error value ?
 4. What is the minimum requirement of the ABPM data for interpretation?
3. Clinical use of ABPM
 1. What is the indications for ABPM?
 2. What is the diagnostic threshold by ABPM, in day, night, and 24 h BPs?
 3. What is the definition of white-coat hypertension and masked hypertension using ABPM?
 4. What is the definition of non-dipper and extreme dipper?
 5. What is the definition of morning surge?
 6. What is the guideline for applying blood pressure variability parameter to clinical practice ?
 7. Which is the preferred between ABPM and home blood pressure monitoring?
 8. What is the clinical opinions for nocturnal hypertension or dipping pattern defined by ABPM ?
 9. What is the role of ABPM as the treatment guidance ?
 10. What is the therapeutic target in ABPM?
 11. Are there any specific recommendations on the Asian perspectives?
4. Barriers against ABPM
 1. Availability of ABPM
 - a. Referral center:
 - (i) Readily available (>75%)
 - (ii) Often available (50%~75%)
 - (iii) Occasionally (25%~50%)
 - (iv) Seldom (<25%)
 - b. Primary care clinic
 - (i) Readily available (>75%)
 - (ii) Often available (50%~75%)
 - (iii) Occasionally (25%~50%)
 - (iv) Seldom (<25%)
 2. Cost for ABPM in USD including battery:
 - a. What is the listed price for a session of ABPM in USD?
 - b. Is it reimbursed by medical insurance?
 - c. If it is reimbursed, is it private or public?

2.3 | Statistical analyses

The proportion of a specific answer to each question was expressed in percentages. The difference in the availabilities of ABPM between primary care clinics and referral centers was tested using the chi-square test with Fisher's exact test for the null cell in the table. The cost per ABPM session was defined as the maximal cost within the range of the cost in each country/region. The difference between the listed cost reimbursed by public insurance and the cost without insurance or reimbursed by private insurance was tested using the Wilcoxon rank sum test or Kruskal-Wallis test. The statistical package SAS 9.4 was used. *P* values of <.05 were regarded as statistically significant.

3 | RESULTS

3.1 | Availability of local guidelines

Among the 11 countries/regions, four had separate guidelines for ABPM;¹³⁻¹⁶ four countries/regions had guidelines for ABPM as a part of their local hypertension guidelines;¹⁷⁻²¹ and the remaining endorsed international guidelines for domestic use.

3.2 | Indications of ABPM: diagnosis of hypertension

There were no recommendations for the routine use of ABPM, as stated in the National Institute for Health and Care Excellence guidelines.²²

The indications common to all countries/regions were diagnosis of white-coat hypertension or masked hypertension and diagnosis of hypertension when clinic BPs are labile or within the borderline (Figure 1). The borderline clinic BP in need of ABPM was specified in only two guidelines: 120-139 mm Hg in Taiwan and approximately 140/90 mm Hg in Japan.

Using ABPM for the diagnosis of white-coat hypertension was primarily based on clinical findings, such as hypertension (clinic BP) with low cardiovascular risk profiles (S), grade I clinic hypertension (V), and clinic hypertension without organ damages (S and V).

Using ABPM for the diagnosis of masked hypertension was primarily based on the presence of organ damages (C, S, Ta, and V) or high cardiovascular risk profiles (C, S, Ta, and V). However, a clinic BP of <120/80 mm Hg was not considered for ABPM in those guidelines.

In relation to HBPM, ABPM was described as the gold standard (C, J, and S) when diagnosis is difficult because the clinic BP and home BP are within the borderline or contradictory, for example, clinic BP of <140/90 mm Hg and home BP of >135/85 mm Hg.

In the clinical context, the timing of ABPM may be differently determined by algorithms for the diagnosis of hypertension. For example, when ABPM is recommended to detect masked hypertension after repeated office BP measurements to confirm that the stabilized office BP is in the prehypertensive range, ABPM must be performed 3-6 months after the initial visit (Ta). On the other hand, ABPM can be performed within a couple of days after initial visit as shown in NICE guidelines.²²

As recommended in most of the guidelines, the indications of ABPM to detect white-coat hypertension or masked hypertension (C, J, K, S, Ta, and V) depend on the presence of organ damage. For example, if the clinic BP is >140/90 mm Hg even after 3 months and there is no organ damage, ABPM is indicated to detect white-coat hypertension in Taiwan.¹⁹ Cardiovascular risk profiles were also considered as an indication of ABPM in the diagnosis of white-coat hypertension or masked hypertension, which were exchangeable with the presence or absence of organ damage (S and V). However, ABPM could be performed as early as possible for

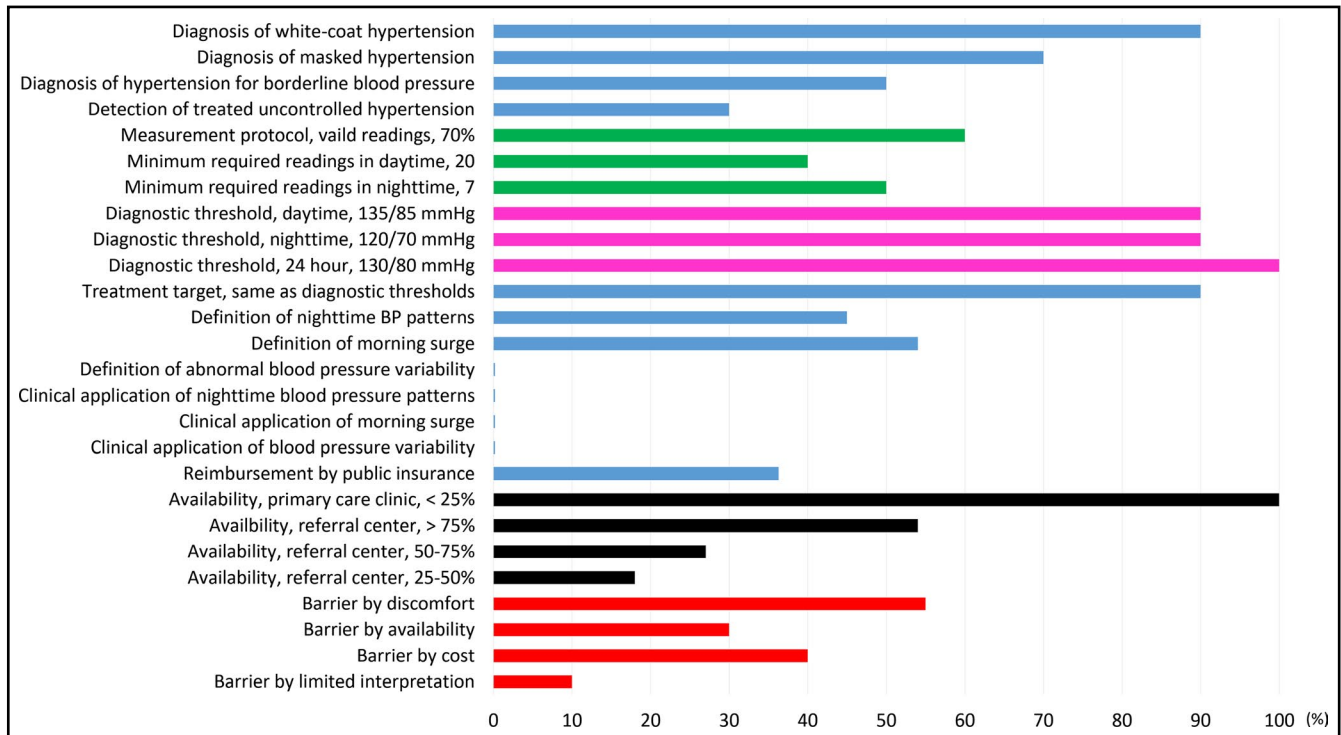


FIGURE 1 Responses to the questionnaire regarding the current use of ambulatory blood pressure monitoring in actual clinical practice in the Asian countries/regions

the diagnosis of hypertension once data on patients' BP and clinical cardiovascular risk profiles are available. For example, ABPM can be considered when the cardiovascular risk is high and when the office BP or home BP is not within the hypertensive range even after 1-2 weeks. In these regards, the recommendation that ABPM is indicated when the home BP is 125-134/75-84 mm Hg makes the timing of ABPM much simpler and consistent with the 2018 ESC/ESH guidelines.^{15,23}

Other specific indications were mentioned in detail, similar to international guidelines.

3.3 | Indication of ABPM: guidance of hypertension treatment

Home BP monitoring is known to increase patient adherence. Most of the guidelines primarily focused on the use of ABPM for the diagnosis of hypertension or resistant hypertension, except for the most recent Chinese guidelines, which directly mentioned treated controlled or uncontrolled hypertension as an indication of ABPM.¹⁶ The other guidelines also mentioned treated hypertension as an indication but in an indirect manner.

3.4 | Measurement protocol for ABPM

The measurement intervals were 15-30 minutes in daytime and 30-60 minutes in nighttime; however, a 60-minute interval was specifically recommended in two countries (M and V). The set time for measurement during daytime was 6 AM or 7 AM to 9 PM, 10 PM, or

11 PM. For the analyses, daytime and nighttime were mainly defined using the patients' diary or mentioned fixed intervals in some countries (C, K, and V), which were variable. Detection of error reading by the device was usually regarded as good enough for clinical use so that additional exclusion or editing was usually not considered. The minimum requirement for the reading was 70% of successful readings with at least seven readings at nighttime in most countries/regions. The 24-hour BP was calculated by device settings by averaging all readings with appropriate time weighting.

3.5 | Clinical criteria or cutoff values

In most countries/regions, the diagnostic thresholds were 135/85 mm Hg in daytime, 130/80 mm Hg in 24 hours, and 120/70 mm Hg in nighttime (Figure 1). However, there were some differences in the preference among the three criteria. Two countries/regions (C and Ta) prefer the threshold 130/80 mm Hg, while the others prefer the threshold 135/85 mm Hg. Fulfillment of all three criteria was needed for the diagnosis of white-coat hypertension in Japan, and any hypertension criteria were enough for the diagnosis of masked hypertension in China.

Nighttime patterns of dipper (10%-20% dipping), non-dipper (0%-10% dipping), reverse dipper (<0% dipping), and extreme dipper BPs (>20% dipping) were indicated in the majority of the countries/regions, and the criteria were exactly the same. Morning surge was defined as sleep-trough surge in six countries/regions (C, J, K, S, Ta, and V). There were no recommended parameters for BP variability for clinical use (Figure 1). Nighttime BP patterns,

morning surge, and BP variability parameters were considered as prognostic indicators; however, no country/region had formal cut-off values recommended to consider morning surge or BP variability for clinical practice.

Although ABPM was mainly indicated for diagnostic purposes, each therapeutic target in ABPM was suggested as the same as the daytime, nighttime, and 24-hour BP diagnostic thresholds in most countries/regions.

3.6 | Perception of Asian-specific needs for ABPM

Most experts agreed that although ABPM may be the gold standard method, HBPM was the preferred option for out-of-office BP measurement because of its feasibility. However, three panels responded with Asian-specific needs for ABPM because of the importance of morning surge, nocturnal BP patterns, and salt sensitivities.

3.7 | Availability of ABPM

In referral centers, ABPM was readily available in seven countries/regions, often available in three countries/regions, and occasionally available in two countries/regions. In primary care clinics, ABPM was seldom available in all countries/regions. There were significant differences in the availability between primary care clinics and referral centers ($P < .0001$).

3.8 | Barrier and cost

Patient reluctance or poor acceptance owing to discomfort by repeated cuff inflations was reported to be a major barrier by six panels (C, K, Pa, S, Ta, and V). In the setting of reimbursement by public insurance, the listed price for an ABPM session was 22.5 USD (interquartile range, 16.5-25.0 USD) (Figure 2). In the setting without insurance coverage or with coverage by private insurance, the cost for ABPM was 100 USD (interquartile range, 50-150 USD), which was significantly higher than that in the setting with public insurance ($P = .0079$, Kruskal-Wallis test).

4 | DISCUSSION

The main finding of our study in relation to the current use of ABPM in 11 Asian countries/regions is that it is used almost exclusively in referral centers. This finding strongly suggests that in the practical approach for measuring out-of-office BPs in primary care settings in Asian countries/regions, ABPM is not currently an option. HBPM might be the immediate alternative as long as devices are available.²⁴ Another important finding of our study is that ABPM is primarily used to diagnose white-coat hypertension or masked hypertension and to measure BP accurately when BP is within the borderline or labile or when clinic and home BPs differ.

However, the clinical algorithm for the detailed timing of ABPM use in terms of repeated measurements of office BP, association

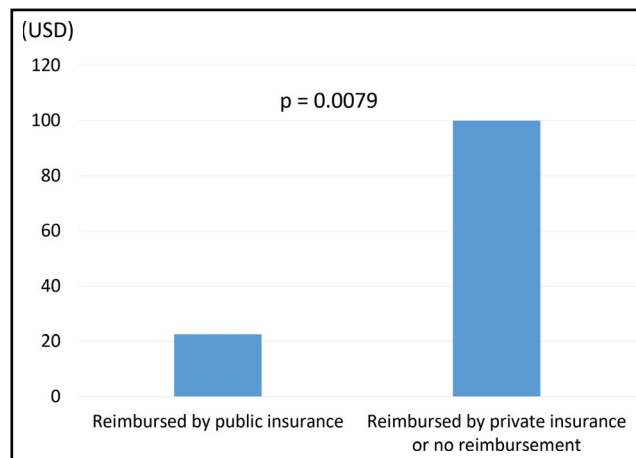


FIGURE 2 Comparison between the listed prices per session of ambulatory blood pressure monitoring when reimbursed by public insurance and when not reimbursed or when reimbursed by private insurance

with organ damages, patients' cardiovascular risk profiles, and priority of HBPM use is not clearly defined. Further, no study has yet investigated the impact of the timing of ABPM on patient awareness or knowledge on hypertension.

In a recent study, the detection rate of masked hypertension in a population without history of antihypertensive drug treatment and clinic BP of $<140/90$ mm Hg was reported to be much higher in ABPM than in HBPM; moreover, the left ventricular mass index was increased only in patients with masked hypertension based on ABPM findings.²⁵ Because of the characteristics of this study population, the conclusion could be generalized easily. Thus, it is imperative to expand the use of ABPM to detect masked hypertension. Particularly, nocturnal hypertension was the most sensitive factor for detecting masked hypertension in this study. Because isolated nocturnal hypertension is also reported to be twofold more prevalent than isolated daytime hypertension in a Chinese population, there is a possibility that nocturnal BP is more important for detecting masked hypertension in Asian populations.²⁶

Because it is primarily used for diagnosis, the application of ABPM for monitoring treatment responses seems to be too limited that only a few panels responded for it. HBPM was the preferred option for this purpose. Recent European hypertension guidelines differentiate masked or white-coat hypertension from masked uncontrolled hypertension (MUCH) or white-coat uncontrolled hypertension (WUCH). These guidelines could be consistent with the 2018 ESC/ESH guideline in terms of the use of the following terminologies: WUCH, MUCH, or sustained uncontrolled hypertension separately from the diagnostic condition.²³ This indicates that out-of-office BP measurement during antihypertensive medication or titration to the target BP is also important. In recent studies, masked hypertension and MUCH, regardless of ABPM or HBPM, showed adverse prognoses, and MUCH diagnosed via ABPM is associated with increased sympathetic activities.^{12,27} In a recent study on ABPM, MUCH diagnosed on the basis of nocturnal BP is twofold more

prevalent than MUCH diagnosed on the basis of daytime BP.²⁸ Thus, in terms of better sensitivity and similar prognostic value, ABPM could be preferred for the diagnosis of MUCH. Moreover, in terms of Asian perspectives, ABPM might be important for some clinical situations, such as morning surge or nocturnal hypertension suspected in high-risk patients.¹¹

Several parameters related to nocturnal BP patterns, morning surge, and BP variability were successfully included in the guidelines in Asian countries/regions; this opinion is quite consistent with international guidelines and the Asian consensus on ABPM.^{11,29} Although there are many reports regarding these parameters, however, the clinical usefulness is currently very limited and more evidence is needed for them to be targeted in hypertension treatment.

Currently, the clinical application of ABPM is largely indicated to the diagnosis of hypertension. Although availability in referral centers was good, and the cost seemed to be reasonable in the majority of the Asian countries/regions, patient factors, such as discomfort, sleep deprivation, and perception or acceptance, were considered the most frequent barrier to performing ABPM. For overcoming these barriers, the guidelines for ABPM should include the method to minimize discomfort or sleep deprivation to maximize patient acceptance. Considering that BP variability is not the primary indication of ABPM in actual clinical practice, the acceptable minimum number of measurements needs to be recommended in the guidelines. In this regard, cuff-less measurement of BP seems to be very promising in the future, although validation issues have not yet been resolved.

Our study is limited to draw firm conclusions regarding the actual clinical setting status of ABPM use in Asian countries/regions because there are only a few studies reporting formal data on such. Nevertheless, our expert panels could present realistic findings on the current status of ABPM use in their respective countries/regions based on their opinion and the study data. Therefore, the approach in our report seems to be the best method to understand the current status of ABPM in these countries/regions. The use of ABPM for scientific research and its practical use in daily practice seem to be quite different; there seems to be much diversity in applying ABPM, and this diversity could induce bias to expert opinions regarding its use in actual clinical practice based on the extent of ABPM research involved. In our report, it was evident that the practical use of ABPM is very simple and straightforward to avoid misdiagnosis and mistreatment. Thus, this difference will not affect the main finding and conclusion of our investigation.

In conclusion, ABPM was used for the diagnosis of white-coat hypertension and masked hypertension and confirmation for borderline clinic or home BPs in the 11 Asian countries/regions. The feasibility was limited mainly by device availability in primary care clinics. The major and minor barriers were patient discomfort and the cost of use when reimbursement by public insurance is not available, respectively. Therefore, considering the gap between these potential benefits and limited use in relation to the availability and feasibility of ABPM, the guideline or consensus for ABPM needs to be simplified according to its practical use, emphasizing the

diagnosis of hypertension and minimizing the number of measurements. More active education for primary physicians and information sharing with patients are also needed; finally, availability and reimbursement should be improved by more recognition by public sectors. For the time being, HBPM might be a reasonable alternative if devices are available.

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AUTHOR CONTRIBUTIONS

JS designed questionnaire, led the survey, performed analyses, and wrote manuscript. KK conceived the project and led the project. YCC, YT, CCH, PB, JN and JS, SH and TK, GPS, JCT, HVM, and JW submitted status report for each countries/regions. KK, YCC, HVM, JW, RD, SS, AAS, YJ, SP, NV, BWT, and TW reviewed each country/region report, reviewed and revised manuscript.

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