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Utility of Blood Pressure Monitoring Outside of the Clinic Setting

Summary

Overview

Elevated blood pressure (BP), also termed hypertension, is a common, powerful, and independent risk factor for cardiovascular diseases (CVD) and kidney disease. Approximately 25 percent of the adult U.S. population, about 50 million persons, has hypertension, defined as current use of anti-hypertensive medication, a systolic BP ≥140 mmHg, and/or diastolic BP ≥ 90 mmHg.

In view of the epidemic of high BP and its complications, prevention and control of high BP continues to be a major national health priority. Governments, institutions, health care providers, insurers, private industry, and non-profit organizations have committed substantial resources to prevent and treat hypertension. Still, hypertension control rates have been unsatisfactory.

Measuring BP to diagnose hypertension and to monitor therapy is problematic. Concomitantly, the enormous scope of the BP problem, the high aggregate costs of hypertension care, and the potential for medication side effects have spawned efforts to target therapy more effectively. This entails identifying lower risk individuals who might be candidates for less aggressive therapy and higher risk individuals who should receive more aggressive therapy. Measurement of BP outside of the office or clinic setting by ambulatory BP (ABP) monitoring and self-measured BP (SMBP) monitoring might accomplish these objectives.

Clinic Blood Pressure Measurements

BP as recorded in the office or clinic setting is the standard technique recommended for measurement of BP in routine medical care. The standard technique includes use of a mercury sphygmomanometer (or a calibrated aneroid device or validated electronic device) and an appropriate-sized cuff. Prior to measurement, patients should rest quietly in the seated position for several minutes. At each visit, at least two readings should be obtained. Except for those individuals with extremely high BP, the diagnosis of hypertension and adjustments in medication should then be based on the average of readings across two or more visits.

Clinic BP measurements have several limitations, even if they are measured according to established guidelines. First, clinic BP measurements exhibit enormous variability, which hinders accurate classification and which frustrates providers and patients. Another limitation is that BP measured in the clinic may not be a representative estimate of usual BP outside the clinic setting. Commonly, BP rises in the clinic setting, in response to the observer and/or other aspects of the medical environment. The difference between measurements obtained in and outside the clinic setting leads to confusion about the diagnosis of hypertension and the need to start or modify therapy. Unfortunately, there are additional limitations because clinic measurements often do not conform to established guidelines. Specific limitations include lack of observer training, inadequate rest period prior to initial measurement, use of wrong-sized cuffs, rapid deflation of cuff, incorrect position of patients, and awkward position of the observer and/or manometer.

Over the past several years, stationary automated devices and aneroid devices have increasingly replaced mercury

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sphygmomanometers in the clinic setting. Aneroid devices are inexpensive but still require an individual, typically a health care provider, to manually inflate a cuff and record the appearance and disappearance of Korotkoff sounds. In contrast, fully automated devices require minimal technical skills, that is, only placement of a cuff and initiation of a reading. An additional reason leading to greater use of aneroid and automated devices stems from concerns over mercury toxicity.

Self-measured Blood Pressure (SMBP)

SMBP devices include mercury sphygmomanometers, aneroid manometers, semiautomatic devices, and fully automatic electronic devices. Automatic devices measure BP using an oscillometric technique in which systolic and diastolic BP are estimated from the pattern of vibrations in the cuff as it is deflated. Fully automated devices are popular because the patient does not have to inflate the cuff or listen for the appearance and disappearance of Korotkoff sounds. Although numerous, perhaps hundreds, of SMBP devices are on the market, very few have been independently validated.

SMBP devices provide an opportunity to record BP at home, outside of the artificial setting of the medical office or clinic. Ideally, the patient is trained to record BP using a standard technique. Occasionally, physicians may observe the patient recording a BP measurement in the clinic and then perform a cross check of readings. The presentation of SMBP data is extraordinarily variable. Commonly, patients at their own initiative provide written lists of readings to their physicians at office visits. However, recent innovations have greatly enhanced the potential utility of SMBP devices to synthesize and present data. Contemporary SMBP devices have the capacity to store and download readings via phone or computer. Data can then be synthesized and reports can be generated and sent to the patient and/or physician.

SMBP has several potential uses. Repeated measurements, if averaged, should provide a more precise estimate of usual BP than occasional measurements obtained in the clinic. As a substitute for clinic BP, SMBP monitoring could then be used to adjust anti-hypertensive drug therapy and thereby reduce the need for frequent clinic visits and their associated costs and inconvenience. The extent to which physicians, or patients, use SMBP data to adjust medication is unclear. In addition, self-measurement of BP has also been proposed as a means to improve adherence with treatment.

Self-measurement of BP theoretically provides a means to diagnose white coat hypertension (WCH), also termed non-sustained or office hypertension. This pattern refers to an elevation of clinic BP in the hypertensive range but normal or low BP outside the clinic setting. Individuals with WCH may be at comparatively low risk for BP-related complications in comparison to individuals with sustained hypertension. An important issue is whether the risk of WCH exceeds that of nonhypertensives.

Ambulatory Blood Pressure (ABP) Measurement

ABP monitoring is a noninvasive, fully automated technique in which BP is recorded over an extended period of time, typically 24 hours. The required equipment includes a cuff, a small monitor (attached to a belt), and a tube connecting the monitor to the cuff. Usually, a trained technician places the device on the patient, provides instructions to the patient, and then downloads data from the device when the patient returns. Most ABP devices use an oscillometric technique. Compared to SMBP, relatively few ABP devices are on the market. However, in contrast to SMBP devices, most currently available ABP devices have undergone validation testing, as recommended by the American Association of Medical Instrumentation (AAMI) or the British Hypertension Society (BHS).

During a typical ABP monitoring session, BP is measured every 15 to 30 minutes over a 24-hour period (including both awake and asleep hours). The total number of readings usually varies between 50 and 100. BP data are stored in the monitor and then downloaded into device-specific computer software. The raw data can then be synthesized into a report that provides mean values by hour and period (daytime [awake], nighttime [asleep], and 24-hour BP), both for systolic and diastolic BP. The most common output used in decisionmaking are absolute levels of BP, that is, mean daytime, nighttime, and 24-hour values. Because of the expense of ABP equipment (up to $5,000 for a monitor, cuff set, and software), the requirement for technicians, the inconvenience and logistics of placing and removing ABP devices, and, until recently, the lack of reimbursement, it is uncommon for ABP monitoring to be done frequently. However, use of ABP will likely increase as a result of the decision by the Centers for Medicare and Medicaid Services (CMS) to cover ABP in selected settings, namely, the identification of WCH.

In addition to mean absolute levels of ABP, certain ABP patterns may predict BP-related complications. The patterns of greatest interest are WCH and nondipping BP. Using both daytime and nocturnal ABP, one can identify individuals, termed nondippers, who do not experience the decline in BP that occurs during sleep hours. Usually, nighttime (asleep) BP drops by 10 percent or more from daytime (awake) BP. Research has suggested that individuals with a nondipping pattern (less than 10-percent BP reduction from night to day) may be at increased risk of BP-related complications compared to those with a normal dipping pattern.

Although ABP could be used to monitor therapy, the most common application is diagnostic, that is, to ascertain an individualís usual level of BP outside the clinic setting and thereby identify individuals with WCH. In addition to detection of WCH, ABP devices may be used to identify individuals with a nondipping BP pattern and to evaluate apparent drug resistance, hypotensive symptoms to medications, episodic hypertension, and autonomic dysfunction. Use of ABP monitoring has been controversial. First, few prospective studies have determined whether this technology predicts cardiovascular disease outcomes and whether this technology provides additional information beyond that of routine clinic measurements. Second, insurers have been concerned that health care providers might overutilize ABP. Third, it has been unclear whether SMBP monitoring is a satisfactory and less expensive alternative to ABP monitoring. Accordingly, health insurers have been reluctant to reimburse for ABP monitoring.

Reporting the Evidence

The utility of BP monitoring outside of the clinic setting was a topic nominated to the Agency for Healthcare Research and Quality (AHRQ) by a group of experts in BP measurement. In September of 2000, the AHRQ awarded a contract to the Johns Hopkins Evidence-based Practice Center (EPC) to prepare an evidence report on this topic. The Johns Hopkins EPC established a team and work plan to develop a report that would identify and synthesize the best available evidence on BP monitoring. One of the first tasks was the identification of an appropriate partner. In December 2000, the National High Blood Pressure Education Program (NHBPEP) of the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH) hosted a working meeting. The NHBPEP includes representatives from national professional and voluntary organizations as well as from Federal agencies. Arising from that meeting was an agreement from the NHBPEP Coordinating Committee to partner with the Johns Hopkins EPC on this project.

A core group of five clinically and/or methodologically oriented technical experts advised the EPC team at key points in the project. This group included experts in ABP monitoring, SMBP monitoring, clinic BP measurement, clinical hypertension, and diagnostic test evaluation. These individuals reviewed draft research questions. Also, this core group along with additional experts in BP measurement and hypertension provided early input at an ad hoc meeting convened by the NHBPEP. The target population consisted of nonpregnant adults with BP in the nonhypertensive or hypertensive range. These individuals are candidates for BP monitoring, and many are candidates for anti-hypertensive drug therapy.

Key Questions

After an extensive deliberative process and with input from the technical experts, the following questions were developed:

- Comparison of clinic, ambulatory, and SMBP readings.
  - 1a. What is the distribution of the BP differences between clinic, ambulatory, and SMBP readings? If there are differences, are these differences reproducible?
  - 1b. What is the prevalence of WCH as defined by SMBP? Is this pattern reproducible?
  - 1c. What is the prevalence of WCH as defined by ABP measurement? Is this pattern reproducible?
- SMBP levels and WCH based on SMBP as related to clinical outcomes.
  - 2a. Is SMBP more or less strongly associated with BP-related target organ damage than clinic BP measurements?
  - 2b. Does SMBP predict subsequent clinical outcomes?
  - 2c. What is the incremental gain in prediction of clinical outcomes from use of self-measurement devices beyond prediction from clinic BP alone?
  - 2d. What is the effect of treatment guided by SMBP in comparison to treatment guided by clinic BP, in terms of:
    - i. BP-related target organ damage
    - ii. symptoms
    - iii. use of anti-hypertensive drug therapy
    - iv. BP control
- ABP levels and WCH based on ABP as related to clinical outcomes
  - 3a. Is ambulatory blood pressure more or less strongly associated with BP-related target organ damage than clinic BP measurements?
  - 3b. Does ambulatory blood pressure predict subsequent clinical outcomes?
  - 3c. What is the incremental gain in prediction of clinical outcomes from use of ambulatory devices beyond prediction from clinic BP alone?
  - 3d. What is the effect of treatment guided by ABP in comparison to treatment guided by clinic BP, in terms of:
    - i. BP-related target organ damage
    - ii. symptoms
    - iii. use of anti-hypertensive drug therapy
    - iv. BP control

- Does the evidence for the above questions vary according to a patient's age, gender, income level, race/ethnicity, and clinical subgroups (e.g., hypertensive/normotensive, diabetic, renal transplant status)?

Methodology

Searching the literature included identifying reference sources, formulating a search strategy for each source, and executing and documenting each search. A comprehensive search plan was developed that include electronic and hand searching. Several electronic databases were searched and a separate strategy was developed for each. First searched was MEDLINE®, which was accessed through PubMed®. Searches using PubMed® were completed in January 2001 and March 2001. The Cochrane CENTRAL Register of Controlled Trials was searched once (Issue 1, 2001). HealthSTAR was searched in February 2001.

Hand searching for possibly relevant citations took several forms. First, priority journals were identified through an analysis of the frequency of citations per journal in the database of search results as well as through discussions amongst the EPC team. Fifteen specialty and general journals were identified. The January to May 2001 issues of these journals were searched. For the second form of hand searching, a database of reference material, identified through an electronic search for relevant guidelines and reviews, through discussions with experts, and through the article review process, was created in the reference management software, ProCite. A listing of titles and abstracts from this database, the BP References Database, was reviewed by the principal investigator to identify key articles. The reference lists of these articles were then reviewed to identify possibly relevant citations. Finally, proceedings from recent conferences were also reviewed.

Abstract and Article Review Process

Specific inclusion and exclusion criteria were applied at each of three levels of review (two levels of abstract review, then article review). Inclusion criteria became more stringent at each level. The titles and abstracts were reviewed for each article identified. During the abstract review process, emphasis was placed on identifying all articles that may possibly have original data pertinent to the questions. For the first-level abstract review, titles and abstracts for all articles retrieved by the literature search were printed on an abstract form and distributed to two reviewers. Because of the extensive volume of literature, a second level abstract review, at which additional exclusion criteria were applied, was necessary. Citations deemed eligible for full article review based on the initial abstract review were printed onto the second level abstract form and distributed to two reviewers.

The purpose of the article review was to confirm the relevance of each article to the research questions, to determine methodological characteristics pertaining to study quality, and to collect evidence that addressed the research questions. Because of the large number of citations that remained eligible for full article review even after the second level abstract review, additional exclusion criteria were applied at the article review level. The final full list of exclusion criteria differed by question. For instance, for question 1a, a comparison of BP by the different techniques, the criterion of more than 1 day of measurement for clinic BP was added because an average clinic BP based on just 1 day of measurements (typically just one to three readings) is extremely imprecise and could lead to a biased comparison with ABP or SMBP.

Article review forms were developed to collect data in a standardized fashion. This process was complex and time consuming due to the heterogeneity of the literature and the diverse questions being addressed. These forms then guided article review. For each of the articles deemed potentially eligible after second-level abstract review, two reviewers read the article, confirmed eligibility status, abstracted key information, and assessed study quality on several dimensions. Because of heterogeneity in study design, data collection forms and elements differed by research question.

Presentation of Results

Evidence tables that summarize aspects of study quality, characteristics of the study population, and features of BP measurement were constructed. For most research questions, these summary tables were similar. However, the evidence tables that display study results differed substantially by research question. Qualitative summaries were prepared which synthesized the evidence and included, to a limited extent, a quantitative assessment (for example, the number/percent of studies with significant associations, overall and occasionally by relevant study characteristics). A draft version of the report was distributed to the partner, the technical advisory group, and other peer reviewers. All substantive comments were collated, the responses of the EPC team summarized, and edits were made to the report as appropriate.

Findings

Key question 1. Comparison of clinic BP, SMBP, and ABP readings.

- *Question 1a. Distribution of BP differences.*

  A total of 18 studies addressed the distribution of BP differences. BP levels measured outside the clinic setting differed from those obtained in the clinic. For both systolic and diastolic BP, clinic measurements exceeded SMBP, daytime ABP,

nighttime ABP, and 24-hour ABP. In the few studies that compared SMBP and ABP, daytime ABP and SMBP appeared similar, while nighttime ABP was consistently lower than SMBP. The literature was insufficient to determine whether these BP differences are reproducible.

- *Question 1b. Prevalence of WCH based on SMBP.*

  A total of four studies addressed this issue. Hence, the literature was insufficient to determine the prevalence of WCH by SMBP.

- *Question 1c. Prevalence of WCH based on ABP*.

  A total of 16 studies addressed this issue. Prevalence varied by WCH definition and study population. Overall, the prevalence was approximately 20 percent among patients with hypertension. Only two studies addressed the reproducibility of WCH. Hence, the literature was insufficient to determine whether WCH based on ABP is reproducible.

Key question 2. The relationship of SMBP levels and WCH based on SMBP to clinical outcomes.

- *Question 2a. Associations of SMBP with target organ damage.*

  Only one study addressed this issue. Hence, the literature was insufficient to determine the associations of absolute SMBP levels or WCH as determined by SMBP with left ventricular mass or proteinuria.

- *Question 2b. Associations of SMBP with clinical outcomes in prospective studies.*

  Only one study addressed this issue. Hence, the literature was insufficient to determine whether absolute SMBP levels or WCH based on SMBP predicts subsequent CVD.

- *Question 2c. Comparison of risk prediction from SMBP and clinic BP.*

  Only one study addressed this issue. The dearth of studies combined with the poor or uncertain quality of clinic BP measurements precluded an answer to this question.

- *Question 2d. Effect of treatment guided by SMBP.*

  Twelve trials addressed this issue, but the evidence was inconsistent. In half of these trials, interventions that included SMBP led to reduced BP. Two trials used contemporary SMBP technology which can store and synthesize SMBP measurements and which can generate BP reports. In both of these trials, the SMBP intervention led to reduced BP.

Key question 3. The relationship of ABP levels and WCH based on ABP to clinical outcomes.

- *Question 3a. Cross-sectional associations of ABP with target organ damage.*

  A total of 25 studies addressed these issues. Left ventricular mass and albuminuria were positively associated with ABP.

- *Question 3b. Associations of ABP with clinical events in prospective studies.*

  A total of 10 studies addressed this issue. In each study, at least one dimension of ABP predicted subsequent clinical events, primarily CVD. In two of these studies, WCH was associated with a reduced risk of CVD relative to the risk associated with sustained hypertension. No prospective study adequately compared the risk associated with WCH relative to the risk associated with non-hypertension. In four of five studies, a nondipping or inverse dipping pattern predicted an increased risk of adverse events.

- *Question 3c. Comparison of risk prediction from ABP and clinic BP.*

  A total of nine prospective studies addressed this issue, but only two studies assessed incremental gain, that is, whether ABP provided additional information that was predictive of risk beyond that of clinic BP. However, the poor or uncertain quality of clinic BP measurements precluded a satisfactory comparison of risk prediction from ABP and clinic BP.

- *Question 3d. Effect of treatment guided by ABP.*

  Only two trials addressed this issue. Hence, the literature was insufficient to determine the effects of treatment guided by ABP.

Key question 4. Findings according to subgroups.

- The vast majority of studies included both men and women, but few studies reported results separately by gender.
- Few studies reported enrollment of African-Americans, and race-stratified data were rarely presented.
- The only notable subgroup finding was a higher prevalence of WCH in women than in men.

In summary, ABP levels and ABP patterns were associated with BP-related target organ damage in cross-sectional studies. Likewise, in prospective studies, higher ABP, sustained hypertension, and a nondipping ABP pattern were associated with an increased risk of subsequent CVD events. Few studies examined corresponding relationships for SMBP. An

inadequate number of clinic BP measurements, as well as the poor or uncertain quality of clinic BP measurements, precluded satisfactory comparisons of risk prediction based on ABP or SMBP with risk prediction based on clinic BP. In aggregate, these findings provide some support for use of ABP monitoring in evaluating prognosis. However, evidence was insufficient to determine whether the risks associated with WCH are sufficiently low to consider withholding drug therapy in this large subgroup of hypertensive patients. For SMBP, available evidence from several trials suggested that use of SMBP can improve BP control; however, further trials that evaluate contemporary SMBP devices are needed.

Future Research

The optimal approach to measure BP remains uncertain. In view of the high prevalence of uncontrolled hypertension, the continuing epidemic of BP-related diseases, and the potential for alternative measurement techniques to improve diagnosis and target therapy, there is a need for comparative studies that assess the relative efficacy, feasibility, and costs of ABP, contemporary SMBP technology, and clinic BP. Specific types of research needs are as follows:

- Prospective observational studies that include SMBP, ABP, and clinic BP. Specific research questions include:
  - What is the repeatability of WCH?
  - What are the risks associated with WCH? In particular, is the risk associated with WCH sufficiently low to justify non-treatment? If yes, in which patients?
  - Does WCH as assessed by SMBP carry the same risk as WCH as assessed by ABP?
  - What are the risks associated with nondipping status?
  - Is nondipping status a surrogate for some other variable that might be measured more easily, that is, without ABP?
  - What is the incremental gain from use of SMBP or ABP over clinic BP alone?
- Clinical trials that test whether contemporary SMBP technology, compared to conventional management by clinic BP, can improve BP control and health outcomes. An additional comparison group might include BP management by ABP. These trials should also compare the aggregate costs of these approaches.
- Decision analyses that determine the costs and effects of strategies that integrate clinic BP, SMBP, and ABP.
- Synthesis of evidence on BP measurements in clinic setting, including issues related to the accuracy and performance of different devices (mercury, aneroid, automated BP) and different observers (physicians, nurses, technicians).

In future research, clinic BP should be measured appropriately by trained observers using validated equipment; measurements should be obtained at several visits. Also, because of the dearth of large-scale, high-quality studies, there is a clear need for government sponsorship of key studies.

To improve the quality of ABP and SMBP publications, standardized methods should be disseminated to researchers and authors. Also, journals should require standardized approaches for presenting ABP data. For published articles, full copies of protocols should be made available, perhaps on the Web. This is especially important because the intense pressure from editors to shorten manuscripts typically leads to reductions in the methods section.

Availability of the Full Report

The full evidence report from which this summary was taken was prepared for the Agency for Healthcare Research and Quality (AHRQ) by the Johns Hopkins Evidence-based Practice Center (EPC), Baltimore, MD, under contract number 290-97-006. It is expected to be available in fall 2002. At that time, printed copies may be obtained free of charge from the AHRQ Publications Clearinghouse by calling 800-358-9295. Requesters should ask for Evidence Report/Technology Assessment No. 63, *Utility of Blood Pressure Monitoring Outside of the Clinic Setting*. In addition, Internet users will be able to access the report and this summary online

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