Methods for Assessing Blood Pressure Values in Humans

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SUMMARY In clinical medicine and epidemiology, measurements of blood pressure largely rely upon the use of cuff inflation and Korotkoff sounds. Although still the most practical, this method has been recognized to have important limitations. This paper focuses on two limitations of the cuff method that have been found while recording 24-hour intraarterial blood pressure in free-living normotensive and hypertensive patients. First, the 24-hour blood pressure is characterized by large long- and short-term variabilities whose magnitudes vary according to the patient's basal blood pressure and age. This is likely to reduce the possibility that a few isolated cuff measurements are accurate and representative of the patient's average blood pressure. Second, during cuff blood pressure assessment by the doctor (and to a lesser degree by the nurse), the patient's blood pressure normally rises due to an alarm reaction, with a large peak within the first 4 minutes and a subsequent decline. The magnitude of the peak rise, as well as its large and unpredictable difference among subjects may be responsible for seriously and variably overestimating the blood pressure. A 10-minute wait from the beginning of the doctor's visit usually avoids this inconvenience. Finally, the paper briefly considers alternative methods to the cuff method, including invasive intraarterial 24-hour recording in ambulatory subjects, which provides a large amount of information but is impractical, and noninvasive automatic blood pressure devices, which offer a promising practical approach but must wait for technical validation. (Hypertension 5 (supp III): III-5—III-13, 1983)

KEY WORDS • invasive blood pressure monitoring • noninvasive blood pressure monitoring • blood pressure variability • hypertension • limitations of cuff method • aging

Since its discovery at the beginning of the 1900s, measurement of blood pressure through cuff inflation at the forearm and use of the Korotkoff sounds is a method used universally in medical practice and in epidemiological studies of hypertension. This method has important limitations, however. Under several circumstances and in several categories of subjects, the readings are inaccurate. Furthermore, they provide only a few values that are barely a tiny fraction of the many thousands of values that occur throughout the day, the mean of which may be quite different. This paper is divided into three parts: 1) data on blood pressure variability are described, which underline the limitations of the cuff method; 2) blood pressure changes that occur during cuff measurements by the doctor are described, which represent an important practical limitation; and 3) alternative methods are outlined, with their pros and cons in the light of our experience.

Blood Pressure Variability

In the late 1960s, Bevan et al. and Stott et al. at Oxford devised a method that allowed patient's blood pressure to be measured intraarterially for 24 hours with limited interference with their ambulation and life patterns. This method enabled them to observe a striking feature of blood pressure, namely, its large variability. Figure 1 shows a 24-hour intraarterial blood pressure recording in an ambulatory patient; it is clear that the blood pressure varied markedly and that variations could last for short and relatively prolonged time intervals.

Over the years, computer analysis of blood pressure has allowed a more quantitative approach to blood pressure variability. Figure 2 shows data from one patient in whom we recorded 24-hour blood pressure by the Oxford method. The computer sampled the blood pressure trace every 60 msec to provide mean arterial pressure (MAP) averages and standard deviations (SD) of each half hour of the recording. The same analysis was performed for systolic blood pressure (SBP) and diastolic blood pressure (DBP) and for heart rate (HR). Half-hour blood pressure averages differed considerably between day and night and between different day periods, and, further, almost each...
average had an SD that showed considerable variation even within the relatively short half-hour intervals. These long- and short-term variations point out the limitations of the cuff method, by showing that not only are blood pressure measurements different in different 24-hour periods, but that they also differ within any given short period of time. This reduces the chance that a randomly taken value can accurately represent the patient's average blood pressure. It should be emphasized that although casual blood pressure is positively related to cardiovascular morbidity and mortality, its predictive value with regard to these complications is limited. This index has been reported to improve with the use of average 24-hour blood pressure values.

Finally, it should be pointed out that the absolute magnitude of long- and short-term blood pressure variations can be markedly different among subjects. The

**Figure 1.** Intraarterial blood pressure recording during a 24-hour period in an ambulatory subject. The recording was carried out via a catheter placed in a radial artery, according to the Oxford method.

**Figure 2.** Computer analysis of systolic, diastolic, and mean arterial pressure, and of heart rate, obtained by a 24-hour intraarterial recording in an ambulatory subject. Points represent average values for each half hour of the recording. The vertical lines indicate the corresponding standard deviations, i.e., the variabilities within half-hour periods. The vertical lines referred to as "a" represent the averages of the half-hour standard deviations, i.e., the measures of the overall variabilities within half hours. The vertical lines referred to as "b" represent the standard deviations obtained by averaging the half-hour mean values, i.e., the measures of the overall variabilities among half hours. These two variabilities were taken to reflect short- and long-term variabilities of the subject (From Mancia and Zanchetti, In Recent Advances in Mild Hypertension, 1982, in press; see ref. 15.)
central and reflex mechanisms involved in these differences have been addressed in a number of studies\textsuperscript{11, 12, 14, 17} and will not be reported here. Figure 3 shows two factors associated with the variability, namely, basal blood pressure and age.\textsuperscript{14, 17, 18} Absolute short-term blood pressure variability showed a significant progressive increase when assessed in a group of subjects with normal or near normal arterial blood pressure, in a group with moderate hypertension, and in a group with more severe essential hypertension (fig. 3, left panel). Absolute short-term blood pressure variability also showed a significant increase in a group of older as compared to a group of younger subjects with similar blood pressure values (fig. 3, right panel). Thus, the error that may be caused by blood pressure variability does not even have an equal "weight" but varies according to the subject's blood pressure and age. This must be considered a further limitation.

**Blood Pressure Changes during Assessment of Blood Pressure by the Doctor**

In hospitalized patients, we investigated the effects on blood pressure of cuff measurements by a doctor.\textsuperscript{19} This was done by recording blood pressure intraarterially for 24 hours and signaling on the blood pressure trace the exact time of the morning visit of a doctor in charge of the routine cuff assessment. The doctor was unfamiliar to the patient and instructed to complete this visit within 10 or 15 minutes. As shown in figure 4, the doctor's appearance was accompanied by an immediate rise in the patient's blood pressure and heart rate, presumably elicited by an alarm reaction.\textsuperscript{20} The blood pressure rise proceeded toward a peak that was usually reached within 4 minutes. The response then declined, the "pre-doctor" blood pressure values being reapproached after the doctor's departure.

Figure 5 shows the peak SBP and DBP increases that were measured in 48 patients during the doctor's

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**Figure 3.** Short-term variabilities of mean arterial pressure (MAP) in three groups of normotensive subjects, subjects with essential hypertension of moderate degree, and subjects with essential hypertension of more severe degree (left panel), and in two groups of subjects (right panel) with an age respectively equal to or less than 38 years (mean 30 ± 1 yrs) and equal or greater than 48 years (mean 54 ± 1 yrs). The 24-hour MAP values at the bottom refer to average MAP values during the 24 hours.

**Figure 4.** Changes in arterial blood pressure during a 10-minute visit of a doctor to make three cuff blood pressure measurements. ABP = pulsatile arterial pressure; MAP = mean arterial pressure; } ABP = arterial pressure integrated at regular intervals of few seconds; HR = heart rate. The arrows at the left and right indicate the doctor's appearance and departure, respectively.
These increases were observed in almost all of the patients although their magnitudes showed an extremely large interindividual difference. However, large responses prevailed over small ones, as the average peak rise in SBP was 27 mm Hg and that in DBP was 15 mm Hg. These large averages make it clear that blood pressure evaluations based on immediate measurements must be avoided. Failure to do so will lead to serious overestimates of blood pressure, and inclusion into hypertension categories people who may be considered hypertensive at the time of the visit only. Two additional factors compound the situation: 1) the large interindividual differences in the magnitude of the doctor-induced blood pressure increase, which prevents an average correction factor to be meaningfully applied; and 2) the individual blood pressure increases do not show any relationship with the patient’s normal or high basal blood pressure, age, blood pressure variability, or response of blood pressure and heart rate to laboratory pressor tests. The correlation of the doctor-induced blood pressure rise with the concomitant tachycardia also appears to be limited ($r = 0.37$). Thus, the error in blood pressure estimation due to the blood pressure reaction to the doctor is both widely different among subjects and almost completely unpredictable in any given subject.

![Figure 5](image_url)

**Figure 5.** Peak increases in systolic (SBP) and diastolic (DBP) blood pressure (obtained from the continuous intraarterial trace) during the doctor’s visit to 48 patients. Data are shown as differences from a control value taken 4 minutes before the beginning of the doctor’s visit.

![Figure 6](image_url)

**Figure 6.** Left Panel: Peak systolic (S) and diastolic (D) blood pressure rises observed in 35 patients during the first and second visit to the same doctor. Central Panel: Peak S and D blood pressure rises observed in 30 other patients during the visit of a doctor and the visit of a nurse. The doctor’s visit preceded the nurse’s visit in 14 patients and followed it in 16 patients. Right Panel: S and D blood pressure increases during the first visit of a doctor in 48 patients, showing peak as well as 5- and 10-minute values during the visit. All differences from a value taken 4 minutes before the visit were statistically significant ($p < 0.01$). Data are shown as mean (± SE) differences.
The final points I will make on the blood pressure reaction to the doctor are in figure 6. The left panel shows the results obtained in 35 patients who underwent two consecutive visits to the same doctor, one in the morning and the other in the afternoon. The average peaks of blood pressure were not significantly different in the two circumstances, indicating that no attenuation of this response and therefore no reduction in the error of blood pressure overestimation can be expected with a simple repetition of the visit. However, this disappointing result is somewhat balanced by the data shown in the other two panels. In the central panel, the rises in SBP and DBP observed in 30 patients during cuff blood pressure assessments by a doctor are compared with that observed in the same patients during cuff blood pressure assessments by a nurse similarly instructed to assess blood pressure within a 10- or 15-minute time period. The increases were significantly less with the nurse than with the doctor, although even the nurse visit did not prevent a significant early blood pressure peak. In the right panel, the time course of the blood pressure responses to the doctor’s visit is shown. After the early peak, the blood pressure declined so that after 10 minutes of the doctor’s visit the SBP and DBP were only a few mm Hg above the values before the doctor’s visit. Because these differences were still significant, an error of overestimation of blood pressure appears to remain even at 10 minutes into the doctor’s visit. It is, however, a much more modest error, and perhaps a clinically acceptable one.

Methods Alternative to the Cuff Method

Present choice is between invasive blood pressure recording and noninvasive automatic or semiautomatic blood pressure monitoring. Invasive recording provides accurate data and complete information within the recorded time, which makes it a valuable tool for hemodynamic hypertension research and for testing the effects of antihypertensive drugs. However, the invasiveness of this method represents an unsurmountable difficulty to its wide practical use, particularly considering that patients are required to be out of sight and control for prolonged times. We have recently examined whether this last inconvenience could be avoided and accurate 24-hour blood pressure averages could be obtained by invasive recordings of more limited duration.

To this aim, the average MAP values obtained during a 24-hour intraarterial recording session were compared with the averages obtained from single hours of recording. The results are shown in figure 7 (upper panel) separately for 28 subjects. In most subjects, averages of the night hours were lower, and averages of the day hours higher, than the 24-hour averages. Regardless of the time of the day or night, however, the differences between hourly and 24-hour averages varied widely (and erratically) from 1 hour to another. Furthermore, these differences always showed a large and variable range among subjects. Finally, the 24-hour averages showed large and variable differences even with the averages of periods as long as 4 hours (fig. 7, lower panel). These findings rule out the possi-
bility of obtaining accurate 24-hour blood pressure values by the restricting invasive recording time to durations compatible with an outpatient clinical service.

My final comments will concern noninvasive automatic blood pressure monitoring. Despite some favorable reports,\textsuperscript{22-24} the accuracy of the blood pressure readings provided by the devices presently available is limited, particularly in free-living subjects.\textsuperscript{25-28} Furthermore, it is unknown whether periodical cuff inflations, and expectation of these events, modify blood pressure. Finally, a theoretical problem might be represented by the intermittency of blood pressure readings. For most devices, these readings can be made at 10- or 15-minute intervals, which amounts to the collection of 150 to 100 values over 24 hours. Because these numbers are still a tiny fraction of the 100,000 values that occur during such time, estimation of average blood pressure might be inaccurate.

We were pleasantly surprised, however, to find that this is not so.\textsuperscript{29} Figure 8 shows individual data of 20 subjects in whom blood pressure was invasively recorded for 24 hours. Each recording was first analyzed beat to beat to obtain the exact 24-hour average blood pressure value. This value was compared with the 24-hour average values obtained by sampling the blood pressure tracing at regular intervals of 5, 10, 15, 30, or 60 minutes. It is clear that in virtually all subjects the average 24-hour values obtained by beat to beat and by intermittent sampling were closely similar, and that in many subjects they were virtually identical. This was the case even when the sampling intervals were increased to 60 minutes (i.e., 24 values in 24 hours). Thus, intermittent sampling does not represent a limitation to the accuracy of blood pressure estimation, and this aspect of automatic blood pressure monitoring stands on a sound basis. Indeed, it seems possible to reduce the number of blood pressure measurements during the 24 hours, making the procedure less troublesome. There is a promising future for this approach, provided that accuracy of blood pressure recordings and the other problems previously mentioned are solved.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure8.png}
\caption{Comparison of average 24-hour mean arterial pressure (MAP) values derived by continuous analysis of the blood pressure trace (one value every 60 msec) and by intermittent analysis that sampled the trace every 5, 10, 15, 30, or 60 minutes. The average value obtained by the continuous analysis is taken as the reference (dashed line) by which differences with the other values were calculated. Individual data from 20 patients. (From Di Rienzo et al., Hypertension 5: 264–269, 1983, by permission: see ref. 30.)}
\end{figure}
Both Professor Doyle and Dr. Mancia have stressed the variability of blood pressure and the difficulty this causes us in defining hypertension and evaluating treatment. Their papers are now open for discussion.
acting as a placebo. That is, the decrease we observe is mainly spontaneous and only to a small degree due to pharmacological intervention. Clearly, both the doctor and the patient are happy with this position and it is often easiest just to continue treatment. Nevertheless, it is sometimes wiser to stop treatment and see what happens. If the blood pressure stays down, then everything is fine. But if it increases again, then the doctor knows that there is a real need for treatment. Of course, this procedure can be done only in cooperative patients — they must not drop from observation.

**Doyle:** I would agree with much of what you say. These drugs do have a placebo effect, and I would go so far as to say that if they produce some side-effects their placebo effect on blood pressure is more likely to be useful.

**Ben-Ishay:** Dr. Mancia, have you got any data on the response of normotensive patients to the arrival of a physician? There is a marked difference between the hypertension-prone and hypertension-resistant rat. When you measure their blood pressure with the cuff method, the hypertension-prone rat always has a much higher blood pressure than the normotensive one, but when you measure blood pressures intraarterially when the rats are at rest, this difference becomes much smaller. Also, their catecholamine concentrations at rest are almost identical, but if the rats are disturbed, the catecholamine levels of the hypertensive rats rise. So possibly the hypertensive individual is simply overreacting to the presence of the doctor.

**Mancia:** The 24-hour blood pressure of our 48 patients ranged from 90 to 150 mm Hg. Over this wide range, we could find no relationship between the basal 24-hour blood pressure value and the response to this particular stress of a doctor's presence. Having said this, let me add that in our study many patients who were found to have relatively low 24-hour blood pressure values had come to hospital because of suspected hypertension. Therefore, our experience with undistinguished normotensive subjects is limited. For ethical reasons, this is so for nearly all studies involving intraarterial blood pressure monitoring.

**Pessina:** Dr. Mancia, do you think that continuous blood pressure monitoring is a substitute for placebo? In other words, could one do away with giving a placebo if one uses this monitoring technique? On your point about the possible rise in blood pressure caused by the cuff inflating, we have been monitoring blood pressure simultaneously with the Oxford system and an indirect method and we found no rise in blood pressure due to the expectation of the inflating of the cuff.

**Mancia:** Thank you for your last comment. It might remove one of the three main problems with the non-invasive approach. As far as your first question goes, a study published in the *Lancet* 2 years ago showed that the placebo effect was present with the cuff method but not when 24-hour recording was performed. We personally have not investigated this point.

**Zanchetti:** Perhaps Professor Doyle would like to say a word about this. Do you think that the fall in blood pressure that you saw in half of the placebo patients was simply reflecting the natural history of these patients, and the disappearance of the alarm reaction that Dr. Mancia described? Or was it really a placebo effect — the consequence of giving a pill?

**Doyle:** It is very hard to separate these two things. The placebo effect is probably due to a quieting of the defense reaction, and this may be achieved either by giving a pill or by habituation. It may be hastened by giving a placebo, but there is no very good evidence of this.

**Zanchetti:** I noticed from your figures that as far as adverse effects are concerned, the placebo effect went to the reverse direction, because the incidence of adverse effects was much greater in the placebo group than in patients who stopped medication or in a sample of the untreated population.

**Doyle:** Yes, there seemed to be a gradation from people not under medical supervision, through to people under medical supervision but not having tablets, to people having tablets whether active or not. I think patients expect when they are given tablets that something unpleasant as well as something beneficial will happen to them.

**Popovtzer:** A plea was made a minute ago that at a certain point during controlled hypertension the doctor may consider discontinuing treatment, to be sure that the treatment is really necessary. I would like to know your opinion about this in the light of the fact that discontinuing treatment may sometimes lead to a dramatic rebound increase in blood pressure, with detrimental effects.

**Doyle:** If the patient's blood pressure has fallen, it does not matter very much whether it is a placebo effect or an active effect as long as both the patient and the doctor are happy. If the doctor is unhappy, he is likely to convey it to the patient, whose blood pressure will then go up. And if he stops the pill, that reaction may make the patient's pressure go up. I personally would leave the treatment alone.

**Salvetti:** It has recently been suggested that the placebo effect on pain is abolished by naloxone, suggesting some mechanism mediated by endogenous opioids. I also have two questions for Dr. Mancia. First, one of your patients showed reduced blood pressure in the presence of a physician. May the presence of a doctor not sometimes provide reassurance and not provoke an alarm...
reaction? Second, how and when should we measure blood pressure in our patients?

Mancia: We cannot exclude the possibility that the doctor’s presence may have a reassuring effect on some patients. However, our observations that in 46 of the 48 patients blood pressure increased when the doctor arrived seemed to indicate that this is a very rare event. As far as your second question goes, if you measure blood pressure after 10 or 15 minutes the chances are that you are close to the values before the doctor arrived — by then the alarm reaction has waned. It is important to emphasize, however, that we do not know, however, which of these values — the later value or the initial, alarm value — is more closely related to cardiovascular risk. Likewise, we do not know whether substituting average 24-hour values for single blood pressure values (and considering factors such as blood pressure variability and reactions to stress) improves the prediction of risk. These are all questions that future research must face.

Doyle: Years ago Smirk showed that the basal pressure correlated much better with outcome than casual blood pressure measurements. But, on the other hand, many of the measurements made for life insurance purposes are casual, and they seem to carry the same sort of effect on prognosis.

Unidentified Speaker: I would like to hear about the response of patients with moderate and severe hypertension to placebo treatment. And what would you recommend for clinical trials? Should there be a 3-month washout period? Should patients with mild hypertension be excluded?

Doyle: Blood pressure is very variable in patients with severe hypertension, and it may fall, but usually it does not fall to normotensive levels. So, although you can demonstrate a placebo effect in severe hypertension, it is not usually large enough to make placebo a substitute for treatment. In milder cases, I believe that 3 or 4 months of observation, reassurance, and salt reduction, if you like, is a sensible preliminary to beginning treatment with active drugs. But there has to be a limit — the higher the blood pressure when you see the patient, the shorter the period should be before you begin treatment. But with diastolic pressures of under 110 mm Hg, I think it is legitimate to keep the patient under observation without active treatment for 2 or 3 months.

Zanchetti: I would like to reinforce this recommendation, which has also been made by the participants in the recent Mild Hypertension Conference organized by the World Health Organization and the International Society of Hypertension (see Lancet 1983; i: 457–8). In patients with mild hypertension, one should not start treatment as soon as it is diagnosed — with values of 95 to 100 mm Hg diastolic — but observe their pressures over 3 months or so.

Silverberg: In the early 1970s, a Czechoslovakian group showed that simple conversation increases cardiac output by 23%. We confirmed this in Israel, and recently Lynch and coworkers have reported the same from the U.S.A. Interestingly, in Lynch’s study the two groups who showed the most exaggerated response to simple conversation were those with the highest pressures and the elderly. My suggestion is that when the doctors walked into the room they started to talk to the patients, which might have increased their blood pressure, whereas the nurses may have just quietly taken the pressure without talking. Were the experimental conditions the same during blood pressure measurement by the doctor and nurse?

Mancia: We tried to mimic conditions as they would be in normal practice; so the amount of conversation depended on the temperaments of the nurses and doctors. Whether the increases we saw resulted from the conversation or from the stress we do not know, but the important epidemiological inference is that when you measure blood pressure with a cuff (and you do this as is normally done in practice) the blood pressure rises.

Silverberg: I would just like to see doctors measuring blood pressure without talking to see whether that makes a difference.

Ledingham: If we come away from this discussion with some firm conclusions, those of us here do not actually have much chance of applying them. Most people here are from hospital and university clinics, whereas the problem we have been talking about is dealt with — at least in England — increasingly by family doctors. The people here exchanging views are not those who will actually be applying the treatment, and that is a problem.
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