

Analysis of 2196 Systematic Blood Pressure Measurements shows highest BP in the evening – An Exceptional Case or Refutation of Generally Accepted Hypotheses?

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Abstract: - An aged male measured his systolic and diastolic blood pressure, left and right, three times a day (morning, afternoon and evening) during a full year under specified conditions and under supervision of both his GP and the authors of the present study. This is the first time that systematic BP measurements of an individual during so many (366) consecutive days have been documented. Analysis of the results indicates that, in contrast to generally accepted views, the highest blood pressure did not occur in the morning (the so-called morning surge) or afternoon (following what is considered to be a circadian cycle for BP), but in the evening. It is also found that the fluctuations in both SBP and DBP are so irregular that momentary values cannot be considered to provide reliable information about the actual blood pressure, and thus about possible cardiovascular risks. Rather, a series of measurements during morning, afternoon and evening should be used. Because this is the first time that such an investigation has been carried out, it can, however, not be fully excluded (though unlikely) that the patient involved represents an exceptional case. Consequently, more comparable studies are needed to confirm or falsify the generic validity of the results found here, which seems of great importance for fighting hypertension and related health risks.

Key-Words: - blood-pressure fluctuations, blood pressure monitoring, circadian cycle, DBP, hypertension, long-term monitoring, morning surge, SBP.

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1 Introduction

Blood pressure (BP) is easy to measure, but there is no precise global figure for the number of annually doctor-performed measurements. The number must, however, be in the billions, given that over 1.3 billion adults have hypertension, and large surveys capture millions of readings.

Obviously, only a small fraction of these data becomes published in accessible literature, but nevertheless thousands of articles and overviews are devoted to blood-pressure characteristics [1] and numerous journals are devoted to this subject. Yet, it is obvious that many aspects of human BP are still insufficiently known.

1.1 Blood-pressure fluctuations

Considering the billions of BP data obtained during routine measurements, it is surprising that there is no general agreement in the medical community about several fundamental aspects. Even though it is generally recognized that both the systolic and the diastolic blood pressure (SBP and DBP, respectively) can show significant fluctuations, both over days and intraday, medical advice on how to deal with this differs strongly. For instance, the Dutch Heart Foundation (NHS) suggests having the blood pressure measured “at least once a year”. Moreover, the various measuring protocols also differ among countries, and even the threshold SBP and DBP values between a healthy blood pressure and hypo- or hypertension may be different [2], in spite of several attempts in the recent past to standardize the protocol for this procedure, e.g., [2], [3], [4], [5].

It is already known for a long time that the fluctuations in BP depend on numerous parameters, such as physical condition, recent physical exertion, diet, temperature, left or right arm, upper arm or wrist, gender, etc. [6], [7], [8], [9]. One of the other parameters that is presumed to influence the height of both SBP and DBP is the time of the day when it is measured. Also, this aspect is, however, under debate.

1.2 A scientific controversy

It is often stated that the BP is lowest in the morning (after an even lower state during sleep), then reaches a peak in the afternoon, to decrease again in the evening (to below the morning values) and further during sleep. This development forms part of the brain-controlled so-called circadian (day-around) rhythm [10], [11], [12].

The presumed fluctuation of the BP controlled by the circadian cycle is based largely on routine measurements of millions (probably even billions) of different people who consulted their GP (one might wonder whether these people form a representative example of a healthy population!).

In contrast, other studies mention that blood pressure is highest in the morning (the so-called morning BP surge [10], [13], [14], which is considered a prediction for a cardiovascular event [15], [16]).

The picture is further complicated by studies that mention that BP is lowest in the morning [17]. This is why major health organizations, including the American Heart Association (AHA), American College of Cardiology (ACC), and the European Society of Hypertension (ESH), recommend blood pressure measurement in the morning (possibly at home) because it reflects the lowest readings before daily activity.

The above controversy must be ascribed to the fact that only a few cases have been documented where the BP of a single individual was measured for a prolonged time, but rarely more than a couple of weeks [18], or with significant interruption [19]. Consequently, no reliable data are available, as far as we are aware, about systematic SBP and DBP measurements of a single individual during a truly prolonged period of time.

It should, consequently, be realized that the current insights into the characteristics of blood-pressure fluctuations are fairly incomplete.

1.3 Objective of the study

The objective of the present study is to find out the fluctuations of the blood pressure of a single

individual during a prolonged period of time. For this purpose, we have carried out such an investigation (see [20] with the help of the individual involved, an aged (79-80 years) male retired professor in one of the natural sciences, who suffered from hypertension, expressed in the form of an uncommonly strongly fluctuating BP. When we discussed with him the steps that he should take (including medication, lifestyle adaptation and BP monitoring), he agreed to measure his BP (SBP and DBP) voluntarily three times a day for a whole year (2024), both at his left and at his right side, if possible within relatively short, fixed periods of the morning, afternoon and evening [20]. As he was still active, he did not want to carry heavy equipment, so it was decided that he should use portable equipment (Tensoval mobile Classic), which was checked before and afterwards for its accuracy.

Some results about the exceptionally long and systematic investigation have been presented before in this journal, regarding the influence of various medications on the hypertension (Supplement; see also [20]) and about the interarm differences [21]. Here we present our findings about the influence of the time of measurement (morning, afternoon, or evening).

2 Methods

For details about the measuring method and its conditions, we refer to [16]. Here we restrict ourselves to some specific details about the times of measurement.

The appointment with the patient was that he should try to measure his BP after having lain down (or at least having sat down quietly) for some minutes; discussions about the best position conclude that both sitting and lying down are appropriate (e.g., [22], [23]). Then he should perform a baseline measurement followed directly by a measurement of his left wrist BP and, again immediately, his right-wrist BP. He should write down the measured values on a pre-printed form, including the date and the measurement time (rounded to quarters of hours, considering the time involved). The morning measurement should take place preferably between 07.00 and 08.00 h, the afternoon measurement between 15.00 and 16.00 h, and the evening measurement between 23.00 and 24.00 h. In order to avoid growing reluctance of the patient against a too strict time schedule, we informed him that this was only a guideline.

We had not expected that the patient would (or even could) hold well to these times, considering his busy life. But, as a scientist aware how important reproducible measurements are, he did very well: of the 366 (2024 was a leap year!) x 3 (morning, afternoon and evening) measurement moments, less than half were out of the intended 1-hour ranges (Figure 1) It must thus be deduced that the data are robust and reliable, but the precise details will be discussed extensively in section 4.3.4.

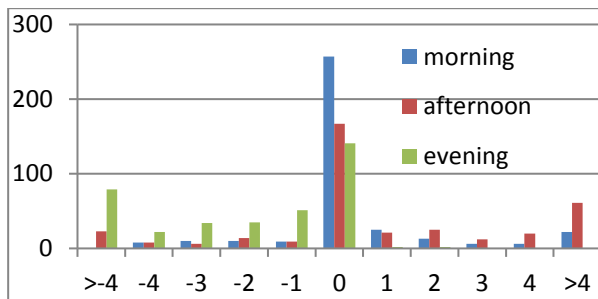


Fig. 1: Spreading of the 1098 measurement moments before, within and after the intended time range. The numbers indicate quarters of a n hour.
Source created by the authors

3 Results

The measurements show some surprising aspects (Figure 2). In contrast with what is stated in the literature, the highest average SBP and DBP values (combined left and right) were not found in the morning, nor in the afternoon, but in the evening (Figure 2). The differences are small: for the three average SBP values they are, respectively, 146.43, 145.36 and 149.13; for the DBP they are 88.73, 88.46 and 90.06).

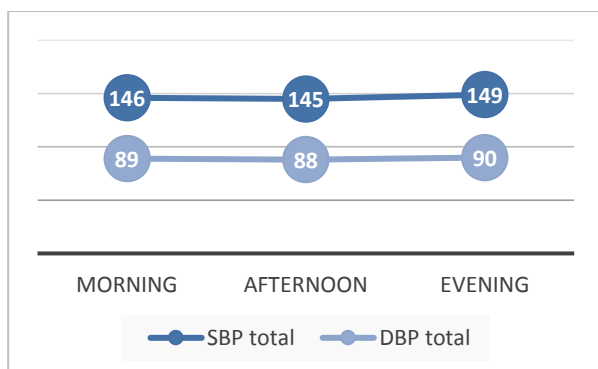


Fig. 2: Average SBP and DBP values (left- and right-wrist values combined) for the morning, afternoon and evening during the 366-day study period. Source created by the authors

3.1 Breakdown into phases with and without medication

The seemingly simple and calm curves in Figure 2 are deceptive: the averaging of the 366 measurements included in each of the 6 measuring points has a damping effect, hiding the variations and thus information about the development of the patient's hypertension. We therefore broke down the data into two sub-groups, viz. for intervals during which medication was administered and for intervals without medication. We did so in order to find out whether the administration of medication significantly changed the blood pressure of the patient during the morning, afternoon and evening. As detailed in Section 3.1 and Supplement, five phases with medication (phases 1, 3, 5, 7 and 9) are separated by four phases (2, 4, 6 and 8) during which no medication was administered to the patient.. Although this approach yielded a different picture (Figure 3), it does, however, still not yield much information. During these intervals, both the SBP and the DBP show some variation over the day, but also here it is obvious that the morning and afternoon are not characterized by the peak suggested by literature [24]. [25], [26], but that the afternoon dip is somewhat better discernible than in Figure 2.

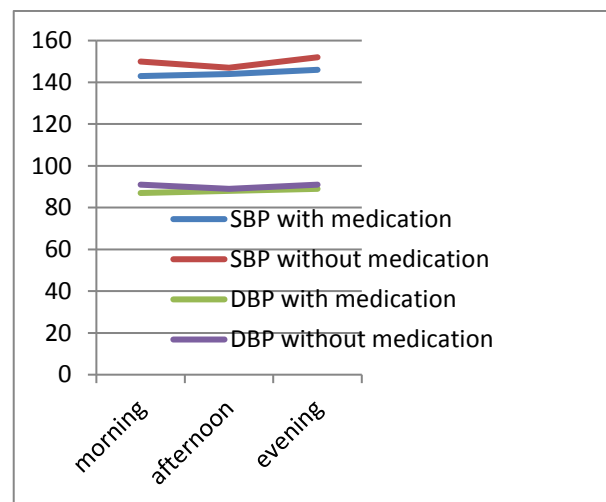


Fig. 3: Average morning, afternoon and evening values for the SBP and DBP (jointly for both the left- and right-wrist values), combined for the phases with medication and those without medication. Source created by the authors

Because the curves in Figure 3 appeared not to show the actual variability of the measured blood pressure, we decided to further break down the data, in order to find out whether a more realistic impression could be obtained if the average blood pressure in each medical phase were calculated.

This was analyzed for both the SBP and the DBP. It appears that this further breakdown provides more interesting information, although The SDP and DPB show different tendencies.

3.2 Breakdown into the individual medical phases

In order to show that the apparently calm and smooth curves of Figure 3 are deceptive, we broke them further down into curves showing the (average) values for each of the nine medication-dependent phases. This is shown for the SBP in Figure 4, which makes the hidden information in Figure 3 somewhat better visible. Figure 4 is, however, still difficult to read (because of curves crossing each other) and even more difficult to interpret.

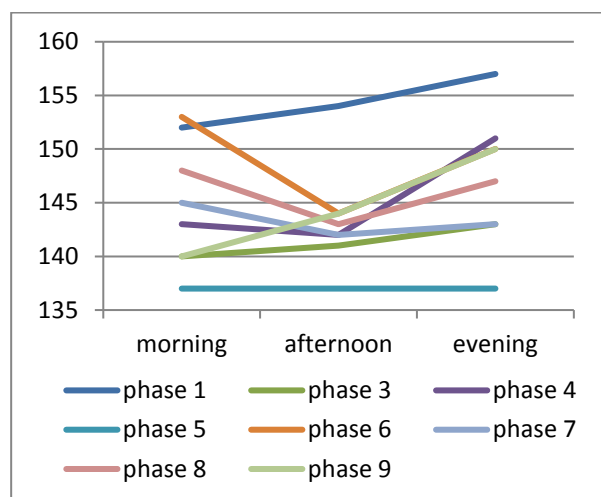


Fig. 4: Average values of the 2196 SBP measurements (left + right wrist) during the 366 measuring days. For explanation of the phases, see Supplement. The 9 phases show fairly large differences for morning, afternoon, and evening, but these differences are partly due to differences in the number of measurements (e.g., for phase 4, $n = 42$; for phase 7, $n = 588$). Source created by the authors

The same holds for the DBP. This part of Figure 3 can also be split up into curves per phase (Figure 5), but the irregular shapes of these curves make this figure, like that for the SBP, difficult to interpret.

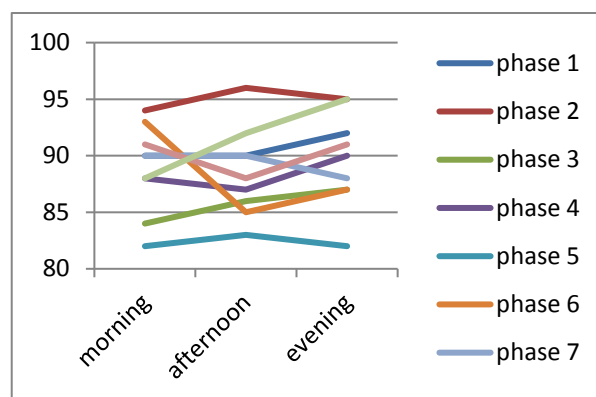


Fig. 5: Average values of the 2196 DBP measurements (left + right wrist) during the 366 measuring days. For explanation of the nine medical phases, see Supplement. Source created by the authors

Therefore, we broke down the curves in both Figure 4 and Figure 5 into curves in two additional figures, one showing the results for the phases with medication (1, 3, 5, 7, 9) and another one showing those for the phases for which no medication was administered (2, 4, 6, 8). These curves are dealt with in Sections 3.2.1 and 3.2.2, respectively.

3.2.1 SBP during the 9 phases

During the 5 phases that medication was administered, the curves show an overall fairly consistent pattern of increase during the day (Figure 6): one curve (5) stays perfectly horizontal, one curve (7) shows a dip in the afternoon, but the other three curves show a continuous increase from morning to afternoon to evening. It thus appears that all 5 curves are in contradiction with the commonly accepted hypotheses of the circadian cycle and the morning surge. This is even more pronounced for the four phases (2, 4, 6, 8) without medication (Figure 7).

All four curves of the SBP during these four phases show a dip in the afternoon; except for one curve (2); in the other curves, the dip is very pronounced. This further challenges the presumption of a circadian cycle with a highest afternoon DBP. Nor do these curves confirm the hypothesis of a morning surge.

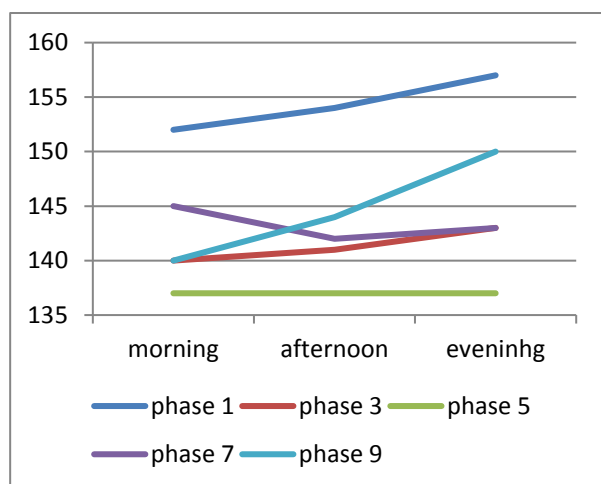


Fig. 6: Average values of the 1776 SBP measurements (left + right wrist) in the morning, afternoon and evening during the five phases that medication was administered. See Supplement for explanation of the medication-dependent phases. Source created by the authors

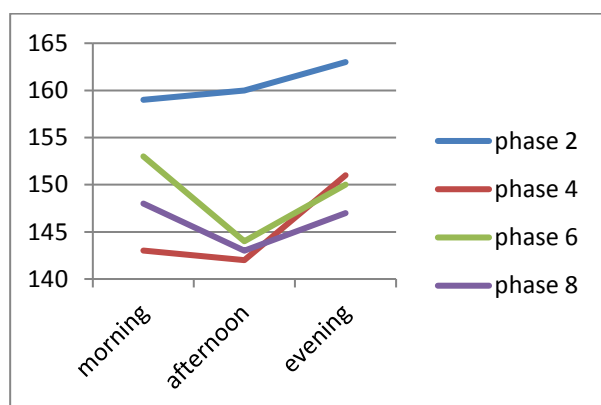


Fig. 7: Average values of the 1776 SBP measurements (left + right wrist) in the morning, afternoon and evening during the four phases that no medication was administered. Supplement for explanation of these 4 phases. Source created by the authors

3.2.2 DBP during the 9 phases

A different view is shown by the DBP. If the measurement results for the nine phases are combined, a relatively chaotic picture arises (Figure 5). The situation becomes clearer if also here the phases with and without medication are presented in separate graphs. The results for the five phases with medication are presented in Figure 8.

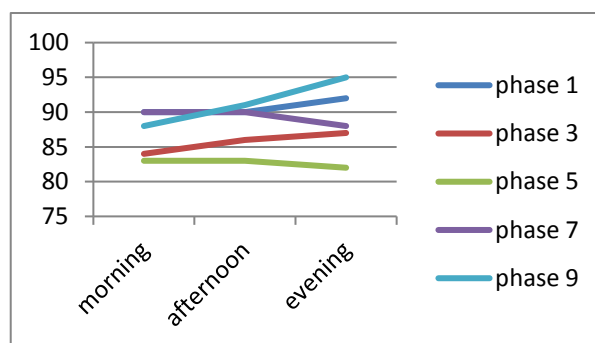


Fig. 8: Average values of the 420 DBP measurements (left + right wrist) during the phases that medication was administered. See Supplement for explanation of the medication-dependent phases. Source created by the authors

This picture is much more complex than the corresponding figure for the SBP because there seems to be no overall tendency; rather, all curves show a different trend, but 3 out of the 5 curves are highest in the evening, thus (again) challenging both the circadian cycle and the morning surge.

The DBP for the four phases without medication (Figure 9) shows an equally complex character. Two curves show an afternoon dip, whereas one curve shows an afternoon peak and one curve has equal morning and afternoon values. Interesting, however, is that only 2 out of the 4 curves reach a peak in the evening.

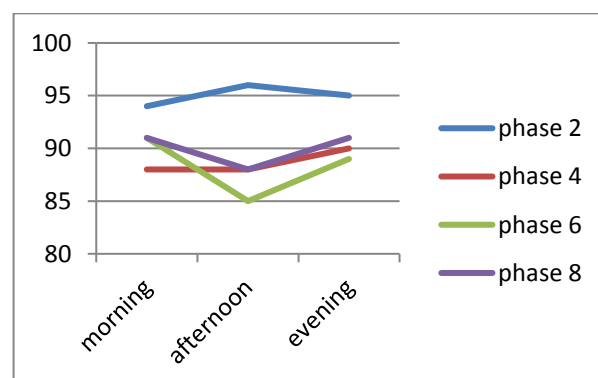


Fig. 9: Average values of the 420 DBP measurements (left + right wrist) during the four phases when no medication was administered. See Supplement for explanation of these 4 phases. Source created by the authors

The complexity of the pictures for the overall SBP and DBP values during the various phases might, due to the applied averaging, hide more actual developments. We therefore decided to present here in more detail the data for one of these phases.

3.3 Further subdivision into data for individual weeks

All above data indicate that averaging of blood-pressure data gives – because of the damping effect that this procedure has – ambiguous data that are difficult to interpret. Obviously, it would be out of scope here to detail all data for the 366 consecutive measuring days, but we feel that it is appropriate to provide here an example in the form of a further breakdown that will show that even the curves showing the averages for the various medication-dependent phases do not provide sufficiently detailed information to draw sound conclusions.

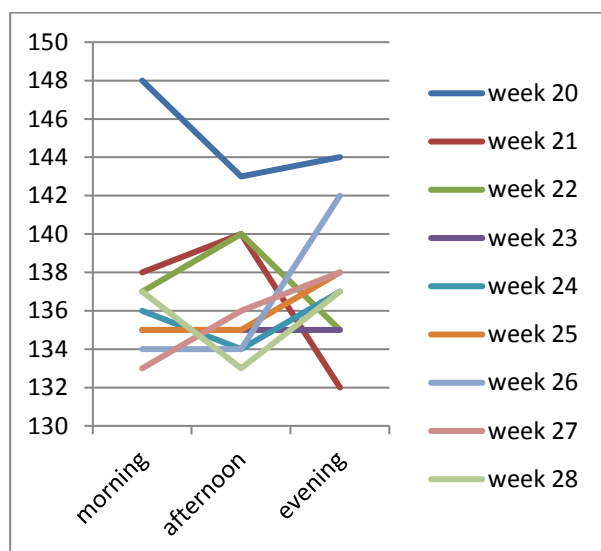


Fig. 10: Daily variation of the average SBP for each of the 9 weeks of medical phase 5. Source created by the authors

For this purpose, we take phase 9 as the example. This phase seems most suitable because it covers 9 weeks, thus providing a sufficiently large number of measurements (189 SBP and 189 DBP measurements) to allow drawing reliable conclusions. Moreover, the SBP shows the same average value (137) for morning, afternoon, and evening, though with a range from 112 to 155; the DBP also shows a consistent rounded average value (83) for morning, afternoon, and evening, but ranges from 112 to 155 (Supplement). The apparently equal average values during the day are misleading, however; the large ranges should already be an indication of possible significant differences between the 9 weeks, and these consist, indeed, for both the SBP (Figure 10) and the DBP (Figure 11).

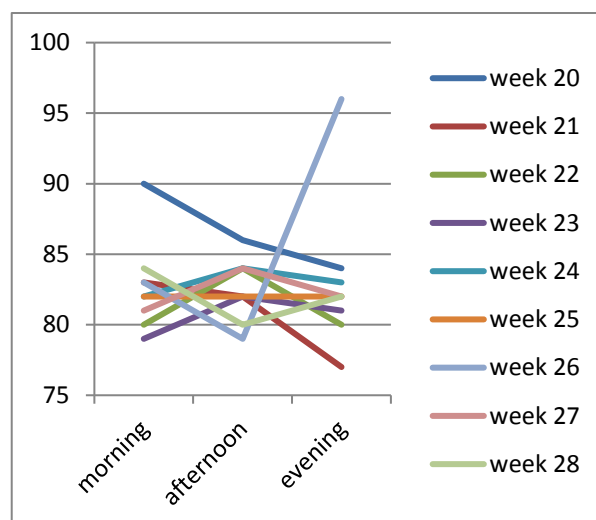


Fig. 11: Daily variation of the average DBP for each of the 9 weeks of medical phase 5. Source created by the authors

It is remarkable how complex Figure 10 and Figure 11 are, although the curves for the average values for the entire phase 5 are both very simple (see Figure 5), with more or less similar values for morning, afternoon and evening. Broken down for the 9 individual weeks, both the SBP and DBP show significant variation. This raises, obviously, the question of whether a further breakdown of the data in these two figures might provide different outcomes. We therefore do so here for the individual days of week 20, the first week of this phase.

3.4 Breakdown of week 20 into its individual days

Although some differences were measured between left and right (see also [20]), these differences were too small during this week to have any influence on the combination of these measurement data presented here. The data for the SBP are presented in Figure 12.

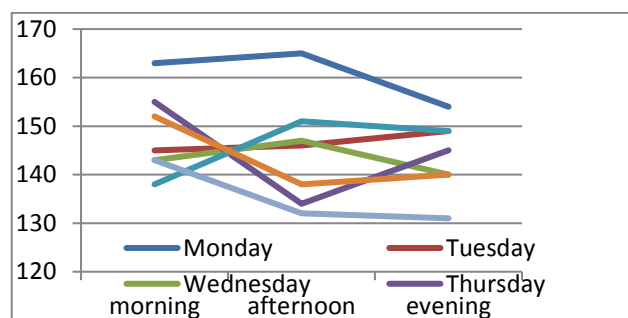


Fig. 12: Daily variation of the average SBP (left and right combined) during the 7 days of week 22. Source created by the authors

It appears that these measurements are just as irregular as the averages for the entire phase 5 (Figure 8 and Figure 10): the Monday, Wednesday and Friday curves peak in the afternoon, whereas the Thursday and Saturday curves then show a dip. In contrast to most curves depicted earlier, only Tuesday peaks in the evening.

The situation is not different for the DBP (Figure 13). Monday and Friday peak in the afternoon, whereas Tuesday and Saturday then dip. No curve peaks in the evening. Note the remarkable difference with the SBP curves.

The examples shown here for the individual days of one week cannot be considered representative. Each week provided different measurement data, implying that data obtained from a limited number of measurements do not give a reliable impression of the actual BP variations of any individual person.

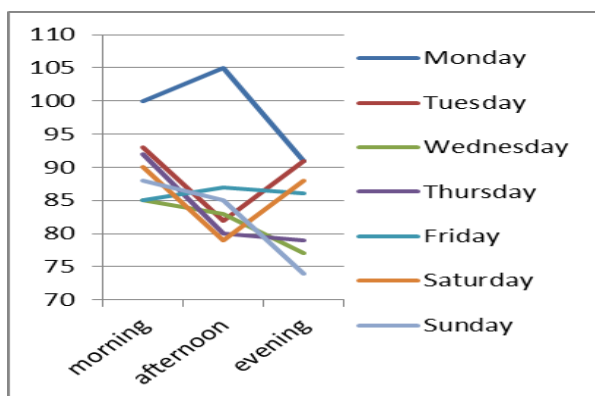


Fig. 13: Daily variation of the average DBP (left and right combined) during the 7 days of week 22.

Source created by the authors

4 Discussion

Analyses of BP measurements require attention for several aspects, particularly (1) the medical background of the patient, (2) the conditions under which the measurements were performed, (3) the choice of the measurement equipment used, (4) the accuracy of the measurements and the reliability of the reported data, (5) the choice of the medication and the duration of the various measurement intervals, and (6) the statistics of the data and their implications. All these aspects have been dealt with in detail in a previous study [20], to which we refer the reader here.

4.1 Time of measurements

Some attention has been paid before [20] also to the time schedule of the measurements, but this parameter requires more discussion here because our finding that the BP shows a tendency to be highest in the evening is surprising: it challenges

present-day views. It should be noticed, however, that two contrasting ideas about the peak in daily BP fluctuations exist: According to the hypothesis of the circadian cycle, the BP (or better SBP) should be highest in the afternoon, whereas the idea of the morning surge states that the peak should occur in the morning.

These two contrasting views already indicate that they are presumptions rather than facts. This is remarkable because billions of BP measurements are made annually. This leads unavoidably to the conclusion that either the measurements are inaccurate, or that the conditions varied, or that there is a bias in the time of measurement. We consider it impossible that the majority of measurements might be inaccurate, even though the American Heart Association states that BP measurements during routine office visits are often taken for granted and can be performed incorrectly 60–70% of the time [27].

4.2 Possible explanations of the peak controversy

The conditions during which most routine measurements are made may well be biased because most BP measurements concern people who visit their GP because they have some health problem. Such patients are, obviously, not representative of the entire population.

Still more important seems the time that most measurements are performed. According to [28], patients primarily see their doctors during the weekdays between 9 a.m. and 4 p.m., with a dip in volume at noon. On weekends, noon appointments are common, representing 15% and 14% of Saturday and Sunday bookings, respectively. This might explain why many routine measurements take place in the morning (with non-healthy patients who may have an increased BP), so that many high-BP measurements are obtained in the morning. This might, at least partly, explain the finding of a morning surge. A comparable situation might explain the afternoon peak: in most countries, GPs visit patients in the afternoon who are too ill to visit their GP. These above-average ill patients probably have, on average, an uncommonly high BP.

Whether or not the two above explanations for the hypothesis of a morning surge and an afternoon peak are correct is not truly essential. Much more important is that the overwhelming amount of BP data is based on momentary measurements of individual patients without a BP context that covers a longer time.

4.3 Time constraints of our data

The above considerations are exactly why we consider our approach (measurement of the BP (SBP and DBP), both left and right, in the morning, afternoon and evening, during a full year (366 consecutive days) much more reliable than the currently commonly applied statistics. This requires, however, some more discussion of the timing of the measurements used for the present study.

As mentioned in the Methods section, the morning measurement should take place preferably between 07.00 and 08.00 h; the afternoon measurement between 15.00 and 16.00 h, and the evening measurement between 23.00 and 24.00 h. Although the patient involved was very interested in this investigation and willing to do his utmost best to adhere to the time schedule, his daily activities could, obviously, not be neglected. He did, however, do very well (Figure 1), but the divergent times need some explanation and discussion here.

4.3.1 Morning measurements

Morning measurements were always done in bed, before the patient stood up. Of the 366 morning measurement moments, 257 (70.2%) were within the preferred range of one single hour. Only 37 (10.1%) were earlier (according to the patient because he was eager to start with some activities), of which 4 (1.1%) were more than one hour 'too early'.

On the other hand, 72 measurements (19.7%) were later than the envisaged time range (according to the patient because he woke up late, due to late activities in the evening or night before). However, 50 (13.7%) of these 'late' measurements were done within one hour after the intended time range.

4.3.2 Afternoon measurements

When at home, the afternoon measurements were done in bed. For this purpose, the patient lay down for a few minutes to come to rest completely before the measurements started.

Almost half (167 = 45.7%) of the 366 afternoon measurements were done within the intended time range. According to the patient, the 'too late' measurements were mostly due to his common outdoor activities (apart from his social activities, he frequently visited scientific and other meetings). In order to keep as close to the time schedule as possible, he did the afternoon measurements sometimes before the intended time range (60 = 16.4%), of which 23 (6.3%) were more than one hour too early.

In spite of these precautions, he came home too late to do the afternoon measurement within the

intended time range 139 times (38.0%). In 61 cases (16.7%) this was even more than one hour, but the measurement values obtained during the 'late' moments appear not different from those obtained 'on time'.

4.3.3 Evening measurements

Evening measurements were always done in bed, when the patient went to sleep. He rested in bed for a few minutes before he started his measurements.

The evening measurements were 141 times (38.5%) done on time. Only 4 (1.1%) were done too late (but never more than 30 minutes), suggesting that the patient took care of his bedtime.

This is confirmed by the numerous times (221 = 60.4%) that the measurements were done before the intended time range. In 79 cases (21.6%), it was even more than one hour before the preferred time range. The patient stated concerning these early measurements that his active life forced him to take sufficient rest, and that it made no sense to him to fall asleep on a chair with an alarm to wake him up when the intended measuring time would have come.

4.3.4 Reliability of our measurements

Although it is commonly recognized that increased blood pressure increases the risk of a cardiovascular event and that blood pressure should preferably be measured when it is at its lowest point, no agreement exists when this lowest point occurs. Several studies mention that a good insight into the blood-pressure height can be obtained only by means of a series of measurements, and that these measurements should preferably be done at home. For this purpose, several such studies have been carried out (e.g., [29], [30], [31], [32], [33], [34]), but none of them has resulted in the documentation of a series of blood-pressure measurements of a single individual of more than maximally a few dozen days. Moreover, the precise times of the measurements are not indicated, so that insight into the systematic distribution of the measurements over the day remains uncertain. Nevertheless, these studies tend to consider home measuring by the patients themselves as providing valuable additional information.

Considering the above, it must be deduced that the measurements described and analyzed in the present study must be considered as scientifically above-standard reliable and useful.

5 Conclusions

An increased blood pressure, commonly in the form of hypertension, forms a severe cardiovascular risk and should therefore be detected as early as possible. This can be done during a visit to the GP, but it is still under debate at what time of the day the blood pressure can best be measured. This debate results from scientific disagreement about when the blood pressure is lowest (the preferred time).

It was therefore decided to take care that the investigation that was started to analyse the effect of various medications on an aged male patient was carried out in such a way that systematic data would become available about the morning, afternoon and evening BP of the patient. This was achieved by an agreement with the patient (a scientifically interested retired professor) that he would measure his SBP and DBP, both left and right, each morning, afternoon and evening. This resulted in 1098 SBP and 1098 DBP measurements.

These systematically obtained data show that, on average, the evening SBP and DBP are higher (though only slightly) than their morning and afternoon equivalents. This is in contrast with the generally adhered to (but mutually contrasting) ideas of a morning surge and an afternoon peak during the circadian cycle. It is argued that the findings of the present study represent the actual situation best (because based on a systematic distribution of measurements over the day), and that the presumptions of a morning or an afternoon peak are based on biases (non-healthy patients and predominant measurements in the morning and afternoon).

Another conclusion is that the fluctuations in SBP and DBP tend to be much larger than commonly assumed, and that these fluctuations do not show any regular pattern. This is proven by breaking down the overall average values into averages per medical phase, then into averages per week, and then into values per individual day.

The findings imply that measuring the BP during a visit to a GP does not give any reliable indication about an increased risk of a cardiovascular or other event. We agree with the studies that state that a larger number of measurements is required for such a prediction, but our study indicates that the number of 14 measurements indicated in previous studies to be required for a reliable prediction of a cardiovascular event is inadequate: our data indicate that such a number can allow a reliable prediction only if consisting of a set of at least 14 measurements in the morning, in the afternoon and in the evening each.

Future studies based on systematic BP measurements spread over the day and made during a prolonged period (at least several weeks, preferably some months) should indicate whether our findings have a generic value or concern (in the form of the patient whose BP was monitored) an exceptional case. The outcomes of such studies will be greatly helpful in reducing cardiovascular risks.

Acknowledgements:

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Data Availability

The complete set of daily measurement data is available from the corresponding author upon reasonable request, but only under specific conditions because of the patient’s privacy and ongoing data analysis by the authors.

Conflict of Interest

The authors have no conflicts of interest to declare that are relevant to the content of this article.

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SUPPLEMENT

Characteristics of the 9 medication-dependent phases during the full-year (366 days, 3 times a day) measurements (simplified from [20]). The indicated medications were administered daily once. Source created by the authors.

phase	medication*	range SBP	average SBP	range DBP	average DBP	duration (weeks)	n
1	L100	130-185	154	73-107	91	13	546
2	none	141-182	161	80-103	95	3	126
3	L100 + Hy25	121-168	141	69-103	86	2	84
4	none	117-168	146	77-100	89	1	42
5	L50 + Hy12.5	116-158	137	68-99	82	9	378
6	no medicine	128-176	150	74-105	88	3	126
7	Hi50	126-163	144	75-107	69	14	588
8	no medicine	121-219	146	70-106	90	3	126
9	Hi50	123-170	145	73-110	92	4 + 2 days	180

* L100 = Losartan 100 mg; L50 = Losartan 50 mg; Hy25 = hydrochlorotiazida 25 mg; Hy12.5 = hydrochlorotiazida 12.5 mg; Hi 50 = Hicrotona 50 mg.