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Random Forest Based Monitoring Approach to Detect Changes in Longitudinal Blood Pressure Data: A Retrospective Study

Uzunlamasına Kan Basıncı Verilerindeki Değişimleri Tespit Etmek İçin Rassal Orman Temelli Bir İzleme Yöntemi: Retrospektif Bir Çalışma

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ABSTRACT Objective: High blood pressure is a serious health condition. Patients and clinicians need tools to early detect deviations from normal blood pressure. Adapting modern methods of monitoring to blood pressure monitoring (BPM) has been a favorable solution. This study focuses on adaptation of machine learning to BPM. The daily chrono-biological changes effect blood pressure and may lead to false alarms in an early detection system. We provide an approach that detects changes in blood pressure with limited baseline data. **Material and Methods:** Our approach uses random forest as an alternative to traditional process monitoring algorithms which test each data point compared to a baseline dataset. In addition, our method converts testing problem into a supervised learning problem using a sliding baseline. We used real data and synthetic data to show the potential of the proposed method for different types of hypertension: sisto-diastolic hypertension, isolated diastolic hypertension and white coat effect. **Results:** Our observations support that the method can detect various patterns such as sisto-diastolic hypertension, isolated diastolic hypertension and white coat effect successfully. **Conclusion:** We described the development of a machine learning based monitoring approach to early detect changes in blood pressure. The proposed method (1) requires relatively small baseline data, (2) can be adapted to real-time patient data, and (3) can detect various types of hypertension.

Keywords: Machine learning; blood pressure; process monitoring; random forest

ÖZET Amaç: Yüksek tansiyon ciddi bir sağlık durumudur. Hastalar ve klinisyenler, normal kan basıncından sapmaları erken tespit etmek için araçlara ihtiyaç duyarlar. Modern izleme yöntemlerini kan basıncı izlemesine [blood pressure monitoring (BPM)] uyarlamak olumlu bir çözüm olmuştur. Bu çalışma, makine öğreniminin BPM'ye uyarlanmasına odaklanmaktadır. Günlük krono-biyolojik değişiklikler kan basıncını etkiler ve erken tespit sisteminde yanlış alarmlara neden olabilir. Sınırlı temel verilerle kan basıncındaki değişiklikleri tespit eden bir yaklaşım sunuyoruz. **Gereç ve Yöntemler:** Yaklaşımımız, her veri noktasını bir temel veri kümesiyle karşılaştıran geleneksel süreç izleme algoritmalarına alternatif olarak rassal ormanı kullanır. Bunun yanında, bizim yöntemimiz, kayan bir taban çizgisi kullanarak test problemini denetimli bir öğrenme problemine dönüştürür. Farklı hipertansiyon türleri için önerilen yöntemin potansiyelini göstermek için gerçek veriler ve sentetik veriler kullandık: sisto-diyastolik hipertansiyon, izole diyastolik hipertansiyon ve beyaz önlük etkisi. **Bulgular:** Gözlemlerimiz, yöntemin sisto-diyastolik hipertansiyon, izole diyastolik hipertansiyon ve beyaz önlük etkisi gibi çeşitli paternleri başarılı bir şekilde saptayabildiğini desteklemektedir. **Sonuç:** Kan basıncındaki değişiklikleri erken tespit etmek için makine öğrenimine dayalı bir izleme yaklaşımının geliştirilmesini tanımladık. Önerilen yöntem; (1) nispeten küçük temel veriler gerektirir, (2) gerçek zamanlı hasta verilerine uyarlanabilir ve (3) çeşitli hipertansiyon türlerini tespit edebilir.

Anahtar kelimeler: Makine öğrenmesi; kan basıncı; süreç izleme; rassal orman

Hypertension is one of the most important risk factors among the preventable causes of death in the world. The increasing incidence of hypertension and as a major outcome cardiovascular disease reveal the importance of continuous monitoring of hypertension. Guidelines for hypertension treatment and control emphases the importance of blood pressure (BP) monitoring.[1-5] High BP is treated with medication and/or habit changes in the patient level. Globally, efforts for early diagnosis of high BP help control the spread of the disease.[2]

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BP monitoring methods are applied for the diagnosis of hypertension and the condition of the patient is determined with the help of the relevant physician.[5] Decision support systems provide support to the doctor in the diagnosis process by comparing the threshold values already determined with the measured BP values. In a typical 24-hour monitoring, it is predicted that BP will be at certain levels depending on the time of day due to the chronobiological nature of the BP. For example, BP and heart rate measurements, which are higher when the person is active during the day, decrease during rest and sleep periods.

BP is generally examined with two main variables as systolic and diastolic BP (SBP and DBP). The existence of a strong statistical relationship between the measurements of these two variables has been known for many years. Process monitoring methods have been widely used in heath surveillance.[6,7] The daily rhythm of the measurements and the existence of a bivariate monitoring problem suggest that the appropriate method for monitoring is multivariate control charts. But the potential of these methods to detect undesired changes in BP limits the use of these methods as they require a long baseline data to estimate the limits of detection. Moreover, in order to monitor SBP and DBP with a multivariate control chart, the usual daytime and nighttime changes (such as the difference between day and night) should be examined separately. In ambulatory monitoring, apart from day and night distinction, two separate methods should be used to monitor the mean (changes in the expected value of BP) and variation (changes due to fluctuation of BP). In this case, for a daily monitoring, at least four multivariate control cards must be operated and interpreted which causes the complexity of decision making.

In this study, the Real-Time Contrasts (RTC) control chart, which is an approach based on random forest (RF) classifier with a sliding window to detect baseline characteristics, and its integration with ambulatory BP monitoring (ABPM) was examined as an alternative to all these problems.[8,9] From this point of view, it is possible to classify the measurements obtained during ABPM for each measurement moment and to measure the probability of having a raised BP measurement. By assigning a threshold value to those using this class probability distribution, observations exceeding this threshold can be assigned as the raised BP. With the proposed approach, 24-hour BP measurements could be classified without distinction of biorhythm, and it was shown by simulation studies that both mean and variation problems could be detected with one control chart successfully. The performance of the method for three hypertensive scenarios (sisto-diastolic hypertension, isolated diastolic hypertension and white coat effect) is shown in the results section. In addition, the performance differences that can be created by the hyperparameter design of the RF classifier have been examined with the experiments. In the study, the caret package was used for open source R software and machine learning applications. Functions and source code in the study were shared over GitHub (https://github.com/eralpdogu/BPMonitor).

MATERIAL AND METHODS

BIORHYTHM OF BP DATA

BP changes over time due to many factors. Most of the time, clinic/office BP checks are not enough to day by day changes. In contemporary clinical practice, a typical 24-hour ABPM is considered as a means of collecting detailed data. Figure 1 demonstrates expected daily changes in BP. This approach increases the ability to estimate mean BP in 24-hours, assess BP variability, and better predict raised BP and ongoing research shows that there is much more information to collect from the 24-hour BP cycle.[10-13] The 24-hour period can be assessed based on a number of windows: daytime, nighttime and morning periods and the transition periods such as daytime to nighttime and nighttime to daytime. Another way to increase the ability to control hypertension is to use a home BP monitoring that spans a larger time period. Thus, it provides deeper information about BP such that long term and short term changes, dietary and prescriptions effects and effects of emotional conditions and seasonality. The periods between day and night and night and day are called vesperal and mantinal windows, respectively. In this study we ignore the measurements observed in these periods (3 hours-before sleep and after wake up) as the values tend to be less reliable.

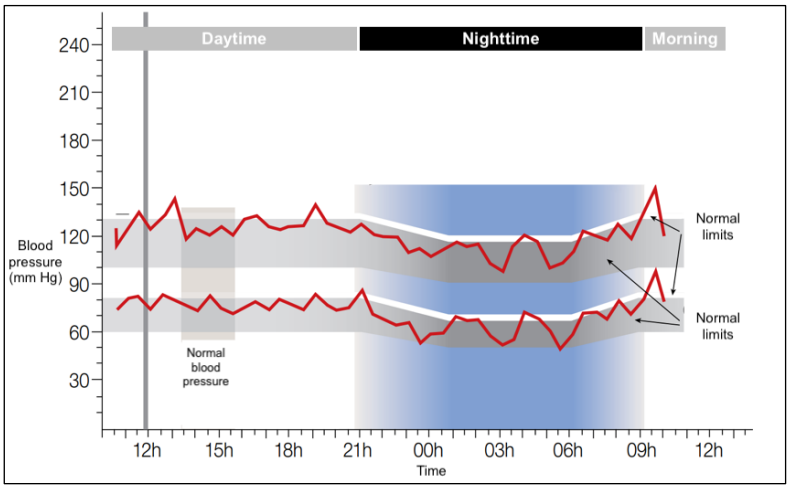

FIGURE 1: Typical blood pressure measurements through 24-hour ambulatory blood pressure monitoring. Changes in blood pressure on daytime, nighttime and morning shows biorhythm of blood pressure through day.

RETROSPECTIVE AMBULATORY BP DATA

The 24-hour ABPM data used in the application belongs to the corresponding author (patient E), a 40-year-old male patient being treated at Muğla Sıtkı Koçman University Research Hospital. As individual data was provided by the corresponding author, the ethical committee approval and informed consent was not needed. The summary statistics are shown in Table 1. Figure 2 shows 44 measurements recorded through ABPM.

TABLE 1: Summary statistics of real-time ambulatory blood pressure monitoring data for patient E.

		Daytime	Nighttime
Sistolic BP (mm Hg)	Mean	124.0	114.0
	Standard deviation	12.9	13.2
Diastolic BP (mm Hg)	Mean	82.0	72.0
	Standard deviation	10.0	13.6

BP: Blood pressure.

In this case, night variation in both BP values was found to be high by the physician and some measurement values during the day were identified as observation of raised BP.

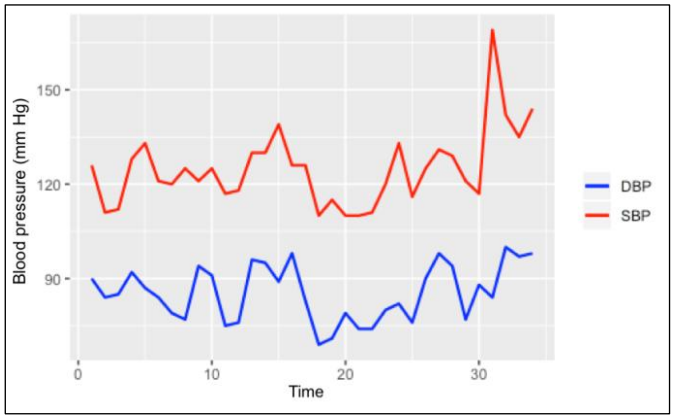

FIGURE 2: Real-time ambulatory blood pressure monitoring data for patient E.
DBP: Diastolic blood pressure; SBP: Systolic blood pressure.

SYNTHETIC AMBULATORY BP DATA

In this manuscript, we also use synthetic data to demonstrate potential uses of the proposed method. First, using patient E's data, we generated a normal daily BP profile for this particular patient. The clinician carefully assessed the dataset and filtered patient's normal BP measurements and we estimated the mean and standard deviation for daytime and nighttime baseline periods. Accordingly, daytime mean SBP was 120 mm Hg, mean DBP was 80 mm Hg, and standard deviation for both periods were 5 mm Hg. Night BP levels for normal condition were determined as 110 mm Hg for SBP, 70 mm Hg for DBP with a standard deviation of 5 mm Hg. For the normal BP profile, random data were drawn from bivariate normal distribution with day and night parameters, assuming that a 24-hour ABPM was performed and a total of 80 measurements were taken in total. Figure 3, Figure 4 and Figure 5 show randomly generated normal BP profiles for three days. We also added a time identifier to this data to stamp each measurement over time. Plus, using the baseline we generated three scenarios of raised BP for this hypothetical patient. We injected raised BP values to the baseline data ($\delta = 15$ mm Hg) for each setting, and used the data to test the method. Research showed that even 10 mm Hg increase in nighttime BP results in 21% increase in mortality risk. Thus, for illustrative purposes we selected 15 mm Hg as the increase amount. We assumed a three day home BP monitoring where the first and third days belong to normal profile (randomly generated from the baseline) and second day being abnormal (disturbances based on δ were injected to the data randomly generated from the baseline). Here, we considered three commonly occurred raised BP scenarios for day 2:

Case 1. High sisto-diastolic BP (test data in Figure 3). Many BP patterns can be distinguished from behavioral ABPM. By far the most common is systo-diastolic hypertension in which both BP levels are generally high during the day and normal at night.[14]

Case 2. High isolated diastolic BP (test data in Figure 4). It is a condition in which the SBP of the patient is normal and DBP is high. Isolated diastolic hypertension can be seen in clinical measurement, but ABPM provides a more accurate prediction of the outcome as well as confirming the diagnosis.[14]

Case 3. White coat effect (test data in Figure 5). The high BP of the patient in the clinical environment is the condition that the BP is at normal levels at other hours of the day. The risk associated with white coat hypertension is controversial, but there is a general consensus that the condition should not be seen as benign, with the risk of developing persistent hypertension.[15-17]

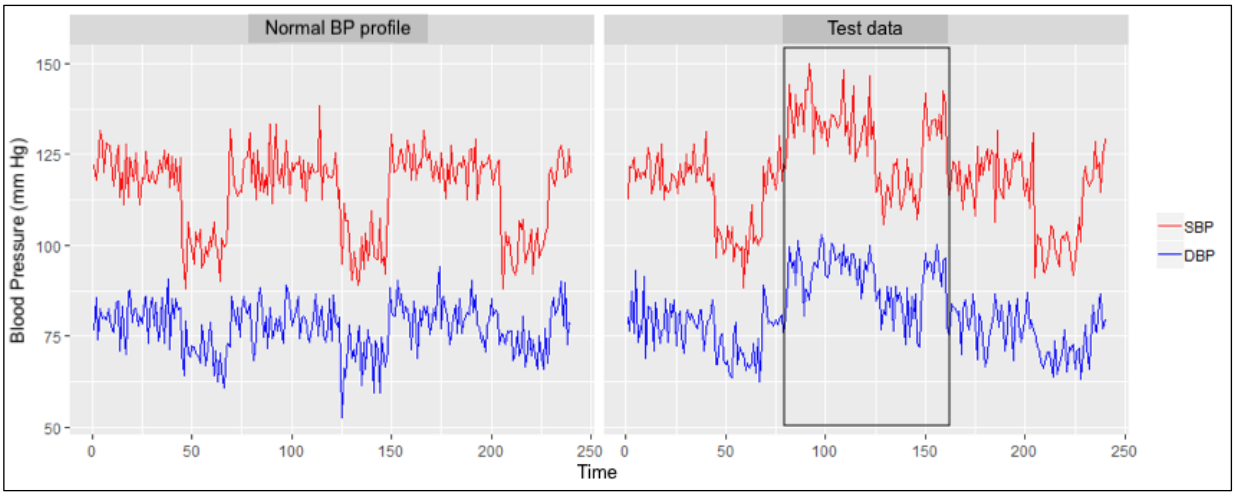

FIGURE 3: Synthetic baseline and test data (three days) for sisto-diastolic hypertension. Black box represents the altered observations. SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

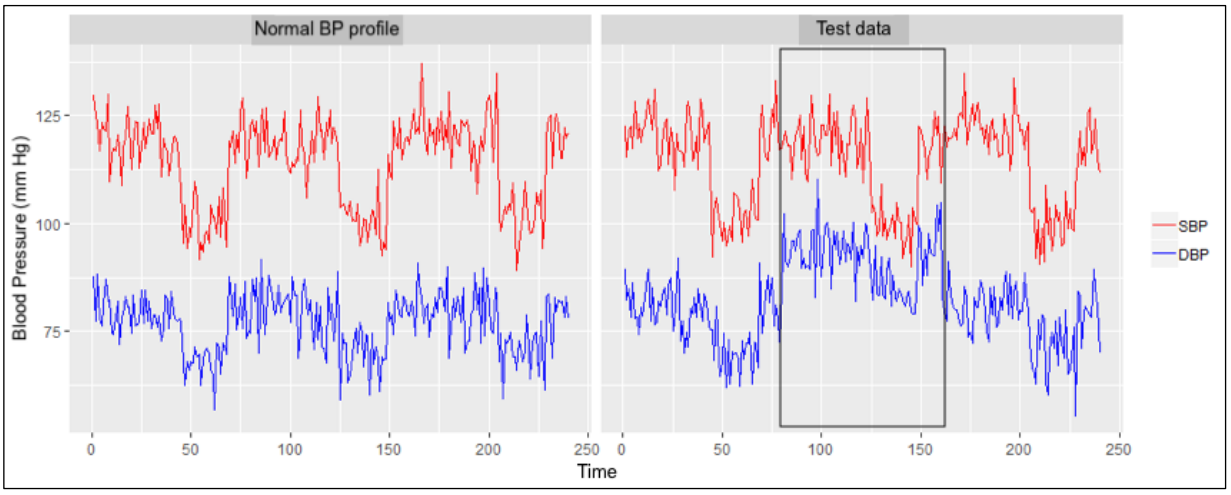

FIGURE 4: Synthetic baseline and test data (three days) for isolated diastolic hypertension. Black box represents the altered observations. SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

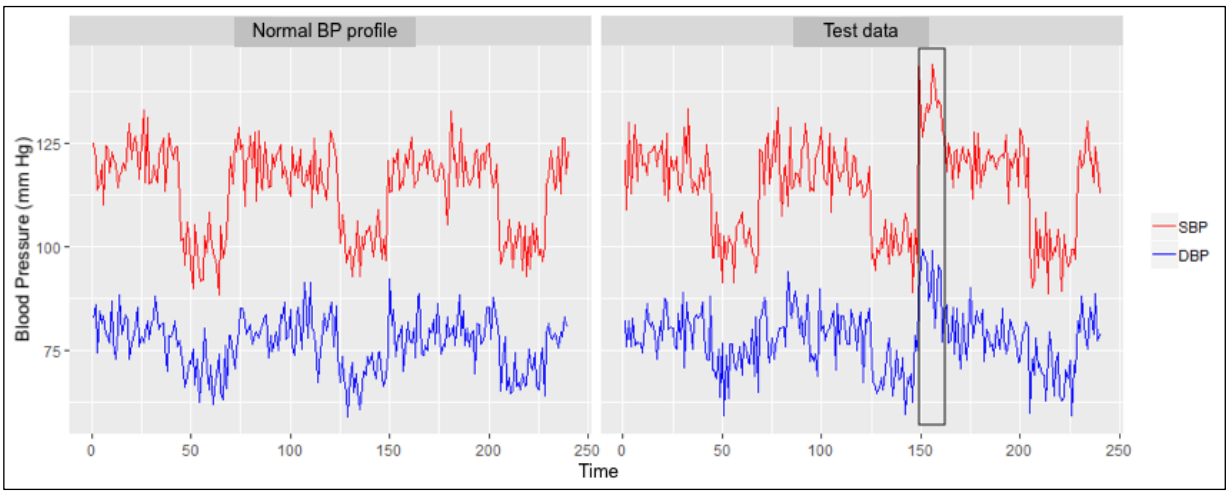

FIGURE 5: Synthetic baseline and test data (three days) for white coat effect. Black box represents the altered observations. SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

RTC CONTROL CHART

Many conventional methods were proposed to monitor longitudinal data.[6,18,19] Implementations to health data provide potential opportunities for disease management and public health surveillance.[6,7,19] These methods mostly rely on a control region showing "normal" estimated based on a baseline data. In practice, however, this assumptions can easily be violated, and this situation degrades the performance of the methods. Classification algorithms are used to create a classification boundary (limit) where class labels (normal or abnormal) are well defined and balanced. Most methods consider baseline data for the fixed boundaries, as the classifiers in methods are only trained once before the start of monitoring. If the off-target state is not properly displayed in historical cohort, the classifier may lose its ability to detect deviations. To solve this problem, RTC control method has been developed.[8] Modifications of this method include.[20-25] Here, real-time data in a window is considered contrast, and RFs form a decision boundary using both baseline data (with only the normal behavior) and real-time observations. This method constantly updates the classification boundary when new measurements are available. RTC assigns a class label to baseline data

and another label to a real-time data window, thereby transforming the tracking problem into a dynamic learning problem. With each new observation, a new classifier is trained and statistics (such as error rate from classifiers) are monitored. Additionally, the RTC chart has advantages (1) user needs to only focus on baseline data with normal behavior rather than trying to collect data for both labels, (2) it can be applied to various types of data, such as categorical data (i.e, time stamp) and missing data, (3) it can be further be used to analyze the causes of abnormality.[20-25]

From each time t, a p-dimensional data vector is obtained and denoted as x_t. It is assumed that baseline data (i.e, first day of test data) from normal BP conditions are available and the sample size N_0 is specified in data matrix S_0. The baseline data is considered a random sample drawn from the distribution $f(x)$. Real time data stream (the second and third days of test data) is $S_w(t) = \{x_{t-N_w+1}, \dots, x_{t-1}, x_t\}$, where t is the current time point and w^{th} sliding window with size N_w. The aim is to quickly detect the changes of x_t from $f(x)$ with a low false alarm rate. Here, a response variable (y) associated with observations at S_0 and S_w at time t can be assigned as $y_{x_i} = \begin{cases} 0, & x_i \in S_0 \\ 1, & x_i \in S_w(t) \end{cases}$. Therefore, an RF classifier with a grid hyperparameter search can sequentially be created on data from two classes. Here, we use a 10 fold cross validation for both model development and threshold calculation. Classification error rates provide information about the control of the process. That is, when there is no drift, the data in both classes are essentially from the same distribution, and then higher error rates are expected. In a shift, if the data comes from different distributions, the error rates are expected to be lower. Consequently, probability estimates will be used for monitoring. At each node in each tree, the m attributes are randomly chosen from the attribute number p. Each of the m attributes is individually scored with a measure of homogeneity, to best separate classes based on a simple rule. Let $\hat{y}(x_i, T_j)$ be the prediction of x_i from the tree T_j. Where $j = 1,2, \dots, T$, OOB_i, is called an out-of-bag (OOB) instance of x_i, and $|OOB_i|$ is the number of trees in OOB_i. Thus, OOB estimation for x_i belonging to the class K$\in$ {1,0}; $\hat{p}_k(x_i) = \frac{\sum_{j \in OOB_j} I[\hat{y}(x_i, T_j) = k]}{|OOB_i|}$. Here I (.) is an indicator function if the argument is true and zero otherwise. As a result, OOB error rates and probability estimates are monitored in this study.

Bootstrap method is used to find the control threshold of the RTC method. The steps of this approach are outlined below.

i. With simulation, normal BP values of the patient are produced. Care should be taken not to have any raised BP observations in this data.

ii. With simulation, the RTC method is run and $\hat{p}_k(x_i)$ values are calculated.

iii. From these values, a B=1000 bootstrap sample is created and % $(1 - \alpha)$ percent of these samples are found. Here α is the type I error probability for the RTC method.

iv. The median of the percentile data set created is calculated and used as the control limit.

RESULTS

PROPOSED METHOD DETECTS ABNORMALITIES IN SYNTHETIC DATA IN VARIOUS BP PROFILES

Case 1: Detection of High Sisto-Diastolic BP

The results in Case 1 data show that RTC method can capture the sisto-diastolic hypertension (Figure 6). The probability of high BP increases after time point 80 as the second day of the dataset was preset to elevated BP. The statistic exceeds the threshold in the whole second day period raising flags for high BP. The statistic kept on being below the threshold in the first and third days showing sign of normal BP. The variable importance values shown below the plot indicates that decision process dominated by first DBP and next SBP.

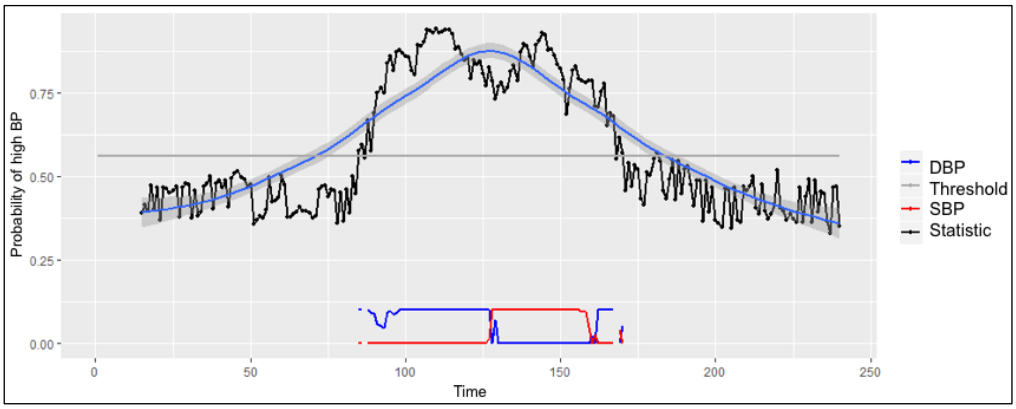

FIGURE 6: Results for sisto-diastolic test data. Sliding window size of 15 measurements. Red and blue lines represent variable importances. DBP: Diastolic blood pressure; SBP: Systolic blood pressure.

Case 2: Detection of High Diagnostic BP

The results in Case 2 data show that RTC method can capture the isolated diastolic hypertension (Figure 7). The probability of high BP increases after time point 80 as the second day of the dataset was preset to elevated DBP. The statistic exceeds the threshold in the whole second day period raising a flag for high DBP. The statistic kept on being below the threshold in the first and most of third days showing sign of normal BP. Some false alarms were also detected in the third day where the method detected higher DBP when compared to normal. The decision process mostly dominated by the DBP which matches the intended design of isolated DBP.

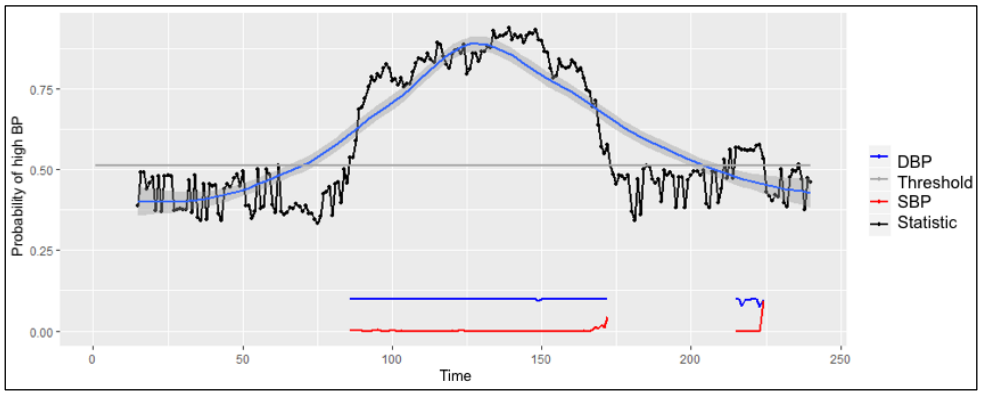

FIGURE 7: Results for isolated diastolic test data. Sliding window size of 15 measurements. Red and blue lines represent variable importances. DBP: Diastolic blood pressure; SBP: Systolic blood pressure.

Case 3: Detection of Isolated High BP Such as White Coat Effect

The results in Case 3 data show that RTC method can capture the elevated BP values resulting from white coat effect (Figure 8). The probability of high BP increases after time point 150 as it was preset in the testing data. The statistic exceeds the threshold in the white coat effect period raising flags for high BP. The statistic kept on being below the threshold in the unaltered measurements showing sign of normal BP. The decision process mostly dominated by the DBP based on variable importance values shown by the blue and red lines generated per time point through sliding windows.

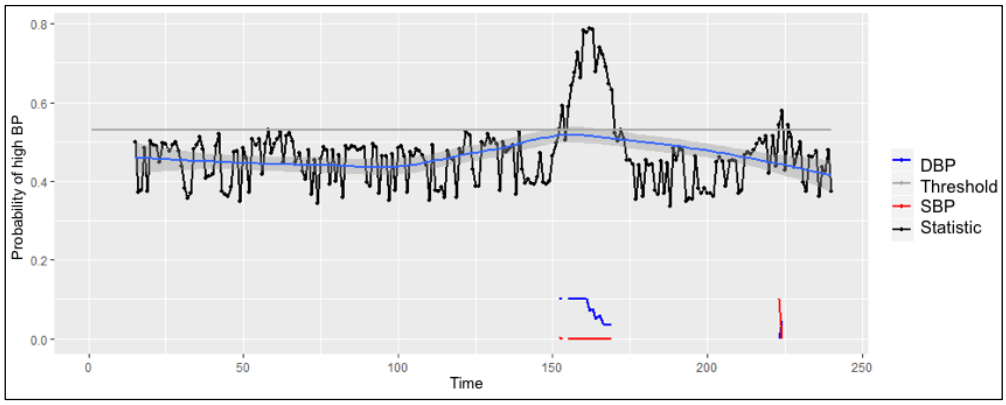

FIGURE 8: Results for white coat effect on test data. Sliding window size of 15 measurements. Red and blue lines represent variable importance. DBP: Diastolic blood pressure; SBP: Systolic blood pressure.

PROPOSED METHOD DETECTS RAISED BP IN REAL ABPM DATA

The results for real-time ABPM data for patient E is shown in Figure 9. When the 24-hour measurement results of the patient are examined; the patient generally suffers from problems due to the increase in DBP especially at night. When the measurements of the patient are examined manually by the clinician, of the 44 measurement values, 16 are flagged as high BP observations. When the same process was followed with the RTC method a window size of 5, we observed 14 matching signals for high BP. We also observed variable importance of DBP is larger than SBP in these measurements similarly to clinician's diagnosis.

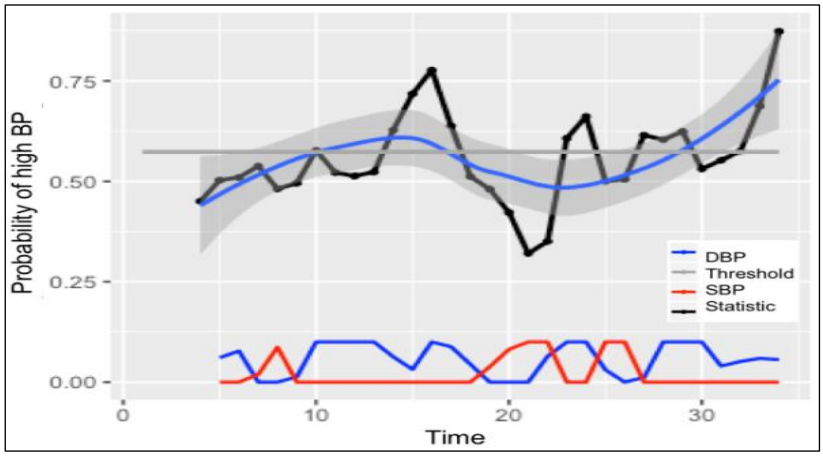

FIGURE 9: Results for real test data.

DBP: Diastolic blood pressure; SBP: Systolic blood pressure.

DISCUSSION

The method we proposed is an integration of RTC chart to longitudinal health data where limited baseline data is available.[8] Other methods such as multivariate self-starting control charts can be used as an alternative to RTC.[6] However, these methods require a multi-conversion method where the feature parameters are estimated by the baseline. Even they work with small baseline data they perform better with larger datasets and require assumptions such as normality.[26,27] In contrast, the method advocated here doesn't require a large baseline data and is distribution free. The method shows satisfactory performance even with a handful of observation.

In order to preserve the effectiveness of the RTC method, the vesperal and mantinal windows observed in ambulatory monitoring were not included in the analysis in this study. This decision, which we support with literature, is due to the fact that these measurement ranges are relatively less reliable than other measurement ranges. In the future studies, these windows can also be modeled and the method can be modified.

Since the RTC method is a method based on RF classifier, it is affected by the hyperparameter design. Since these choices affect the performance of the method, it is important to determine the optimal values. This situation, which was demonstrated only with a grid search for small-scale experiments in this study, may be examined in detail in future studies. The hyperparameters also affect the computation time. It is recommended to prefer hyperparameter designs that can calculate class probabilities in a short time enough and at the same time with high performance. Our machine learning algorithm selection was based on but there are other variations such as monitoring with support vector machines, with RF based on weighted voting or with kernel distances.[8,23,28,29] As our aim is to integrate the method to longitudinal BP monitoring, we kept the original recipe. In future work, other classifiers may be compared. Another important research direction could be the selection of sliding window size which was fixed to 15 which makes approximately four hours. The experiments we conducted show slight differences between sizes 10-20, however, further research should be considered for optimal size depending on the data acquisition design.

CONCLUSION

In this study, we proposed the use and integration of RTC method for early diagnosis of hypertensive attacks in BP monitoring. Simulations show that the method successfully reveals the possibility of high BP and that these findings are consistent across various hypertensive crisis scenarios. The method tests whether the measurements come from the normal BP distribution with the help of sliding windows and repeatedly based on the patient's normal BP values. In this case, it can be said that the length of the sliding windows directly affects the performance of the method. Our trials have shown that it would be appropriate to choose longer window lengths for patients with the potential to experience long-term high BP and shorter window lengths for patients with the potential to experience isolated high BP.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and/or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Eralp Doğu, Hilmi Fidan;* ***Design:*** *Eralp Doğu, Hilmi Fidan;* ***Control/Supervision:*** *Eralp Doğu, Hilmi Fidan, Tuğba Dübektaş Canbek;* ***Data Collection and/or Processing:*** *Eralp Doğu, Hilmi Fidan, Tuğba Dübektaş Canbek;* ***Analysis and/or Interpretation:*** *Eralp Doğu, Hilmi Fidan, Tuğba Dübektaş Canbek;* ***Literature Review:*** *Eralp Doğu, Hilmi Fidan, Tuğba Dübektaş Canbek;* ***Writing the Article:*** *Hilmi Fidan, Eralp Doğu;* ***Critical Review:*** *Hilmi Fidan, Eralp Doğu;* ***References and Fundings:*** *Hilmi Fidan, Eralp Doğu, Tuğba Dübektaş Canbek;* ***Materials:*** *Eralp Doğu, Tuğba Dübektaş Canbek.*

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