Quantification of Nocturnal Blood Pressure Oscillations Induced by Sleep Disordered Breathing

Yao-Shun Chuang, Mahrshi B. Jani, Armin Soltan zadi, Raichel M. Alex, Rong Zhang, Donald E. Watenpaugh, Khosrow Behbehani

Abstract— **We present an approach to quantifying nocturnal blood pressure (BP) variations that are elicited by sleep disordered breathing (SDB). A sample-by-sample aggregation of the dynamic BP variations during normal breathing and BP oscillations prompted by apnea episodes is performed. This approach facilitates visualization and analysis of BP oscillations. Preliminary results from analysis of a full night study of 7 SDB subjects (5 Male 2 Female, 52±5.6 yrs., Body Mass Index 36.4±7.4 kg/m^2, Apnea–Hypopnea Index 69.1±26.8) are presented. Aggregate trajectory and quantitative values for changes in systolic blood pressure (SBP) and diastolic blood pressure (DBP) concomitant with obstructive apnea episodes are presented. The results show 19.4 mmHg (15.3%) surge in SBP and 9.4 mmHg (13.6%) surge in DBP compared to their respective values during normal breathing ($p<0.05$). Further, the peak of the surge in SBP and DBP occurred about 9s and 7s, respectively, post the end of apnea events. The return of SBP and DBP to baseline values displays a decaying oscillatory pattern.**

Clinical Relevance— **Nocturnal blood pressure oscillations are considered detrimental to cardiac health. Quantitative assessment of these oscillations can be useful in monitoring the health of sleep apnea patients.**

I. Introduction

The most common sleep disordered breathing (SDB) is obstructive sleep apnea (OSA). OSA is characterized by repetitive cessation or reduction in inspiratory airflow to the lungs due to upper airway obstruction during sleep [1]. It is estimated that as many as 18 million adults in the U.S. maybe suffering from OSA [2]. There is approximately a 2:1 higher prevalence of OSA in men compared with women [3]. This ratio is even higher (i.e., 8:1) in the population of individuals who have been referred to sleep labs for diagnosis of OSA [3]. A drop or dipping in the blood pressure (BP) during a night of sleep is important for health [4]. However, this pattern seems to be altered in OSA patients. The non-dipping pattern is considered as a marker of future development of hypertension [5]. Moreover, the increased variation in nocturnal blood pressure is a characteristic of nocturnal hypertension in OSA patients [6]. Such a phenomenon is due to a temporary increase in arterial stiffness resulting from sympathetically mediated vasoconstriction, or increased cardiac stroke volume driven by isotropic effects of sympathoexcitation, or both [7]. Our group as well as others have reported highly repetitive and significant surges in BP during apnea in OSA patients. A study using intra-arterial BP monitoring or continuous finger BP measurements reported that an apnea event causes an acute transient BP elevation at the time of its termination, resulting in high BP [8].

Importantly, studies have found that cardiovascular events are more prevalent during sleep in OSA patients compared with non-OSA persons [9, 10]. This is attributed to a non-dipper pattern of nocturnal BP and nocturnal hypertension in OSA patients which are significantly associated with increased risk of cardiovascular disease [9]. Hence, ways of accurately quantifying nocturnal BP dynamic changes during sleep are useful for measuring the severity of BP oscillations and ultimately assessing the health risks of such oscillations.

In this paper, we present an approach to quantitatively aggregate the large number of nocturnal BP oscillations elicited by apnea events. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) trajectories following apnea events are used to obtain aggregate measures reflecting the effect of apnea over the course of sleep.

II. Method

A. Experimental setup

Seven subjects (5 Male 2 Female, 52±5.6 yrs., Body Mass Index, [BMI], 36.4±7.4 kg/m^2, apnea–hypopnea index, [AHI], 69.1±26.8) who were referred to our collaborating accredit sleep laboratory (Sleep Consultants Inc., Fort Worth, TX) for diagnosis of sleep apnea volunteered for the study. The subjects signed a written consent form that was approved by our Human Subject Institutional Review Board. Sensors for full polysomnography (PSG) study were attached to each subject. These included external nasal pressure sensing cannula, chest and abdomen respiration plethysmography bands, electro-encephalography, electrocardiography, electrooculogram and electromyography electrodes, and finger oximeter probe. In addition, the finger cuff of a continuous blood pressure monitor (Nexfin monitor, BMEYE, Amsterdam, Netherlands) was placed on either the ring or middle finger to concurrently and continuously measure the blood pressure throughout the PSG study. After the completion of PSG study, a certified sleep technician, blind to the objectives of this study, scored the PSG data and identified the apnea episodes.

B. Selection of Apnea Episodes for Analysis

To quantify the effects of individual apnea events on the nocturnal BP, we opted to consider apnea episodes that were

Y. Chuang, M. Jani, and K. Behbehani are with the Bioengineering Department at the University of Texas at Arlington (kb@uta.edu); A. Soltan-zadi is with Alcon, Fort Worth, TX; R. M. Alex is with Brigham and Women's Hospital, Boston, MA; D.E. Watenpaugh is with Studio Videnda, LLC, Fort Worth, TX; Rong Zhang is with Texas Health Presbyterian Hospital and Neurology and Neurotherapeutics Department at UT Southwestern Medical Center, Dallas, TX.

978-1-7281-1990-8/20/$31.00 ©2020 IEEE

at least 30 s apart from the next respiratory event. Fig. 1 illustrates an example of an apnea episodes that was analyzed from one of the subjects. As shown, the apnea event is not succeeded by another apnea event for at least 30s. In Fig. 1, the arrows labeled with -30s and +30s denote the temporal width of the interval over which we analyzed the blood pressure (BP) values to capture the impact of each apnea episode. As shown in Fig. 1, we interpolated the systolic and diastolic values of blood pressure pulses (red and green envelopes, respectively) resulting using a cubic spline interpolation function. The resulting SBP (red) and DBP (green) envelope were used for aggregating the BP variations.

C. Establishing Blood Pressure Baseline

To assess the impact of apnea episodes on the nocturnal blood pressure, we first needed to determine the basal blood pressure level when no apnea is present. To accomplish this,

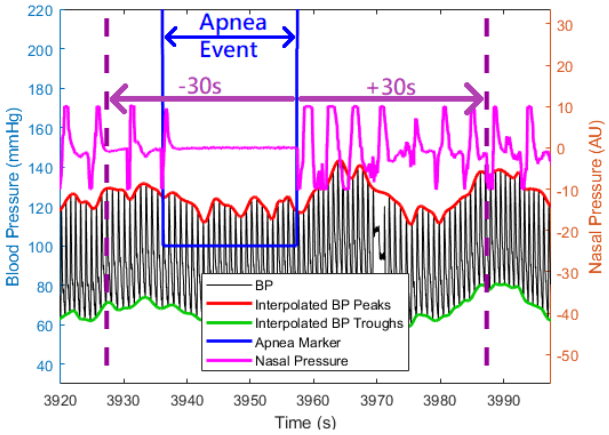

Figure 1*: A representative apnea event that was used in the analysis for this paper. The arrows marked with -30s and +30s represent the temporal width of the interval over which the blood pressure was analyzed.*

for each patient we identified one minute of normal breathing during the night where no SDB was present. The beat-to-beat blood pressure pulses during this interval were analyzed to extract SBP and DBP trajectories; referring to these trajectories as SBP Baseline and DBP Baseline. To obtain aggregate SBP and DBP Baselines for the subjects, the individual subject SBP and DBP Baselines were respectively averaged using a sample-by-sample averaging.

D. Computing Effect of Apnea Episodes on Blood Pressure

Considering the high importance of systolic and diastolic blood pressure values for clinical applications, we focused on quantifying the impact of apnea episodes on these two measures. To this end, we set the end point of all selected apnea episodes (Fig. 1), to be the zero time point and performed a sample-by-sample averaging of the SBP and DBP trajectories for 30s prior and 30s post the end point (shown with double-head arrow labeled as -30s +30s in Fig. 1) To obtain an aggregate measure of BP oscillations for each subject, the averaging of SBP and DBP was done for each subject separately. Further, we did a sample-by-sample averaging of all SBP trajectories of the selected apnea episodes and for all of the subjects to obtain an aggregate trajectory of the SBP for the sample population. Similarly, the same averaging was performed for the DBP. In addition to obtaining sample-by-sample mean values, we also computed the 95% confidence interval (CI) for each averaged sample values of SBP and DBP. As shown in Fig. 1, in almost all instances of analyzed apnea episodes, the blood pressure peaks after the termination of the episode.

III. RESULTS

Fig. 2a shows the one-minute SBP Baseline recordings during normal breathing (no apnea) for all subjects. Fig. 2b displays the average and 95% CI resulting from the aggregation of the values shown in Fig. 2a. Similarly, Fig. 2c shows the one-minute DBP Baseline recordings during normal breathing for all subjects and Fig. 2d shows the average and 95% CI resulting from the aggregation of the values shown in Fig. 2c. In contrast, Fig. 3a displays a plot of the SBP trajectories during all apnea events in the sample population which were separated from the next apnea event by at least 30s. There was a total of 221 of such events for the subjects and Fig. 3b shows the result of aggregating these trajectories as well as the corresponding 95% CI. Similarly, Fig. 3c displays a plot of all the DBP trajectories for the same 221 apnea events. The results of aggregating these DBP trajectories and the corresponding 95% CI are shown in Fig. 3d.

The first row of data in Table 1 shows the aggregate results from all subjects, while the rows below that show the results for each of the 7 subjects. Specifically, the entry in the 2nd column for the first row shows the average and standard deviation of all sample-by-sample values of the SBP Baselines for all subjects (Fig. 2a). The entry under Col. 3 in the first row of the table shows the average and standard deviation of the peak SBP values during all apnea events (Fig. 3b). The magnitude and % deviation of the mean for the SBP during apnea event from baseline mean are shown under Col. 4 and Col. 5, respectively. The temporal location of the SBP peak is at 9s (first row Col.6). Column 7 shows the total number of apnea events that contributed to the results show in each row. The corresponding values of the entries just described for individual subjects are presented in rows labeled No. 1 to No.7 in Table 1.

Table 2 contains the metrics for DBP values. Using the DBP trajectories, all entries in Table 2 were obtained in the same manner as those described for Table 1 above.

IV. DISCUSSION

Examining the Baseline SBP values and the Baseline DBP their aggregate averages (Fig.2) reveals that patients in the sample population had an overall relatively stable BP during normal breathing. Indeed, the standard deviations of SBP and DBP of the Baseline for the subjects (Table 1&2, Col.2, subjects No.1-7) are between 1.4 to 5.8 mmHg.

Table 1- Systolic Blood Pressure Variations

Col. 1	Col. 2	Col. 3	Col. 4	Col. 5	Col. 6	Col. 7
Subject	**Mean Baseline SBP (mmHg)**	**Mean Peak SBP during Apnea (mmHg)**	**Difference of Mean Peak and Baseline SBP (mm Hg)**	**% Difference of Mean Peak and Baseline SBP**	**Temporal Location of SBP Peak (s)**	**No. of Apnea Events Averaged**
ALL	127.3 ± 14.5	146.7 ± 21.6	19.4	15.3%	9.0	221
NO. 1	120.1 ± 4.2	133.2 ± 15.6	13.1	10.9%	10.2	34
NO. 2	141.2 ± 5.8	158.8 ± 9.7	17.6	12.4%	6.0	49
NO. 3	114.9 ± 4.0	140.8 ± 23.1	26.0	22.6%	9.9	17
NO. 4	138.4 ± 3.2	173.3 ± 13.2	34.8	25.2%	14.5	42
NO. 5	118.4 ± 4.3	137.4 ± 13.0	19.0	16.1%	6.0	44
NO. 6	148.2 ± 4.0	160.4 ± 17.6	12.2	8.2%	15.6	16
NO. 7	109.5 ± 3.5	120.7 ± 8.4	11.2	10.2%	10.6	19

Table 2- Diastolic Blood Pressure Variations

Col. 1	Col. 2	Col. 3	Col. 4	Col. 5	Col. 6	Col. 7
Subject	**Mean Baseline DBP (mmHg)**	**Mean Peak DBP during Apnea (mmHg)**	**Difference of Mean Peak and Baseline DBP (mm Hg)**	**% Difference of Mean Peak and Baseline DBP**	**Temporal Location of DBP Peak (s)**	**No. of Apnea Events Averaged**
ALL	68.9 ± 6.6	78.3 ± 10.6	9.4	13.6%	6.6	221
NO. 1	66.8 ± 2.5	80.2 ± 10.1	13.4	20.1%	7.2	34
NO. 2	67.2 ± 2.3	77.8 ± 4.3	10.5	15.8%	5.8	49
NO. 3	68.8 ± 3.0	85.9 ± 17.6	17.1	24.9%	9.9	17
NO. 4	70.4 ± 1.4	82.7 ± 6.6	12.3	17.5%	11.6	42
NO. 5	76.2 ± 2.7	85.1 ± 11.3	8.9	11.7%	6.2	44
NO. 6	76.2 ± 1.9	74.1 ± 5.8	-2.2	-2.8%	25.0	16
NO. 7	56.8 ± 2.6	64.2 ± 6.3	7.5	13.0%	8.2	19

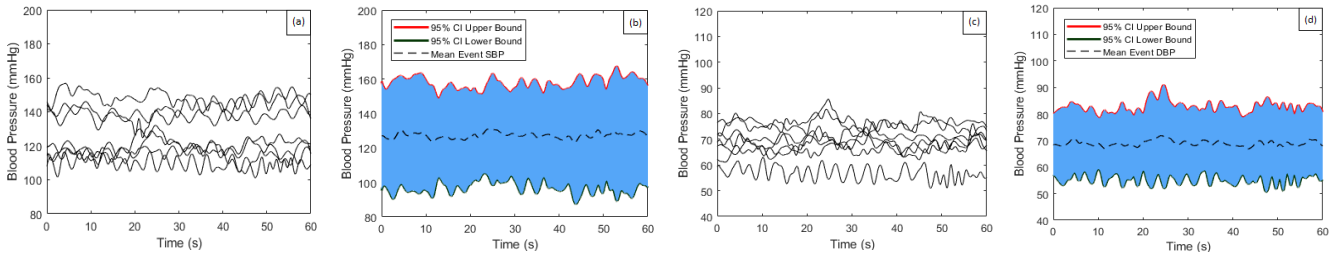

***Figure 2**: Aggregated Baseline of blood pressure signals from all the subjects: (a) Systolic blood pressure (SBP) Baseline recordings for each of the 7 subjects; (b) Aggregated SBP Baseline with 95% confidence interval envelope; (c) Diastolic blood pressure (DBP)Baseline recordings for each of the 7 subjects; (d) Aggregated DBP Baseline with 95% confidence interval envelope*

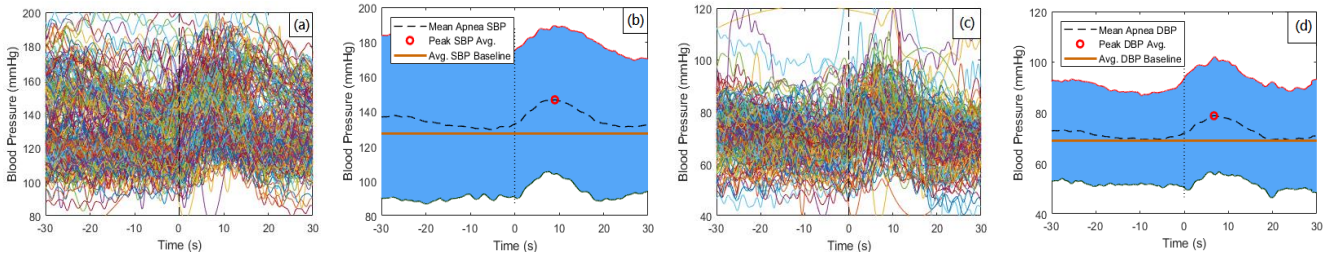

***Figure 3**: Aggregated blood pressure oscillations elicited by apnea events: (a) Systolic blood pressure (SBP) recordings for all analyzed apnea events for all subjects; (b) Aggregated SBP oscillations elicited by apnea with 95% confidence interval envelope (shaded area); (c) Diastolic blood pressure (DBP) recordings for all analyzed apnea events for all subjects; (d) Aggregated DBP oscillations elicited by apnea with 95% confidence interval envelope (shaded area)*

This is in contrast with the distinct oscillations observed in both SBP and DBP associated with apnea events that can be seen in Figs. 3b and 3d, respectively. The level of the oscillations in the BP post selected apnea events is reflected in the sharp rise in the mean and the standard deviation of SBP and DBP values (Table 1&2, Col. 3, subjects No.1-7) which shows that the peak of the average of SBP surges over 19 mmHg (>15%) and average of DBP surges by almost 9 mmHg (>14%) with respect to their respective Baseline average values. The t-test of the mean values for the Baseline SBP and the peak SBP elicited by apnea (Fig. 3b) showed that they are significantly different ($p<0.001$). Similarly, the test of the means for the Baseline DBP and DBP peak (Fig. 3d) showed that they are significantly different ($p<0.001$). The greater variations in the blood pressure elicited by apnea events results in a relatively wide 95% confidence interval envelopes in Figs. 3b and 3d, indicating that the expected range of oscillations can be in excess of 50 mmHg. Such large oscillations in the

nocturnal BP would be of interest to clinicians as they may have health implications. Specifically, the repetitive and large nocturnal surges in BP can lead to organ damage and cardiovascular events [10]. These surges can lead to a rise in catecholamine and impairment of baroreceptor sensitivity. These physiological reactions may eventually affect the daytime BP rhythm and blood pressure variability.

Considering Figs. 3b and 3d, it can be observed that the peak of oscillations that are induced by apnea events do not occur within the apnea interval, rather they occur after the apnea has ended. As Table 1&2 show, the average delay for SBP and DBP to peak is approximately 8s. Another observation of interest from Figs. 3b and 3d is the average trajectory of the BP changes elicited by apnea events. As can be seen, the trajectory of the SBP and DBP returns toward the Baseline after peaking are oscillatory, indicating underdamped overall BP restoration control to the pre-apnea level.

V. Conclusion

Analysis of continuous nocturnal blood pressure for a sample of sleep apnea patients showed large oscillations are elicited by apnea events. These oscillations tend to have peaks that occur after an apnea event has ended, rather than within the time interval that apnea is in progress. The observed large magnitude of oscillations elicited by each apnea event suggest that they could have clinical significance.

Acknowledgment

This work was partially funded by a grant from the Department of Energy. The contribution of Dr. Scott A. Sands who initially introduced the authors to a general aggregation method is gratefully acknowledged.

VI. References

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