Validation of Pulse Transit Time Based Blood Pressure Estimation on Atrial Fibrillation Patients

Yang Chen[1], Shoulin Huang[1], Tong Wang[1], Ting Ma[1,2,3,4 *]

Abstract— **Pulse transit time (PTT) based continuous cuff-less blood pressure (BP) monitoring has attracted wide interests owing to its potential in improving the control and early prevention for cardiovascular diseases. However, it is still impractical in large-scale clinical application due to the concern of BP measurement accuracy. Since such approach strongly relies on the PTT-BP model under certain theoretical assumptions, the accuracy would be affected by the vessel properties alterations induced by cardiovascular disorders. Atrial fibrillation (AF) is one of the most common cardiac diseases which often coexist with hypertension. The present study sought to examine the Impact of AF on the PTT and BP, validate the capability of PTT based cuff-less methods on AF patients. By investigating the PTT and BP on 74 critically ill patients with AF, we found that parameters including PTT, R-R interval and diastolic BP (DBP) were significantly changed when AF occurs, while the systolic BP (SBP) value and photoplethysmography intensity ratio (PIR) changed little. Further, by performing two cuff-less BP estimation method, we found that the estimated accuracy is decreased on PTT based method when AF occurs, but there is little change on PIR based method. The findings demonstrated that the impact of AF on PTT is significant, which would also influence the PTT-BP relationship. But the PIR would still be a predictive factor for BP estimation for AF patients.**

I. INTRODUCTION

Cardiovascular diseases (CVDs) are among the leading causes of death worldwide according to the reports by the World Health Organization. Evaluated blood pressure (BP) is a key risk factor for CVDs, and it would result in significant financial and health burden[1]. Regular long-term BP monitoring is a valuable tool that is employed to improve BP level control and has a prognostic meaning for hypertension[2]. However, traditional cuff-based BP measurements include the auscultatory and oscillometric techniques are underused by hypertensive patients performing self-monitoring because of the effort involved as well as the discomfort caused by the repeated cuff inflations and deflations.

Comparing to cuff-based measurement, the cuff-less approach can achieve a more comfortable and effortless BP monitoring, thus enhancing patient compliance with respect to self-monitoring and promoting improved cardiovascular health. Therefore, cuff-less technologies have attracted much attention. The most general and sophisticated cuff-less BP measurement technique is pulse transit time (PTT) based BP estimation. PTT based BP estimation is based on the pulse-wave propagation theory and the Moens–Korteweg (M–K) equation, which could be described using the following equations.

$$\mathrm{PTT} = \mathrm{L} * \sqrt{\frac{\rho d}{Eh}} \tag{1}$$

$$\mathrm{E} = E_0 e^{rP} \tag{2}$$

where L is the length of the vessel, E is the elastic modulus of vessel, E_0 is the elastic modulus when the vessel inner pressure is 0, h is the vessel thickness, ρ is the density of blood, d is the inner diameter of the vessel, γ is a constant related to the particular vessel, and P is the inner pressure of vessel, which is also known as BP. PTT-BP relationship has been widely investigated [3, 4], and current PTT-BP relationship is under the following assumptions: (1) vessel properties including ρ, γ, and the ratio of h to d remain constant; (2) wave reflection interference is absent[5]. Thus, the major factors that affect the PTT-BP relationship are the vessel elastic modules, the inner vessel diameter, and the vessel wall thickness. Accordingly, vessel properties alterations induced by the cardiovascular disorder would distort the PTT-BP relationship[6]. Previous studies have investigated patients with chronic heart failure and found that the PTT-BP relationship was impaired in those patients[7, 8]. It is reasonable to hypothesize that the cardiovascular disease would potentially affect the PTT-BP model and may have a significant impact on the accuracy of PTT based BP estimation.

Atrial fibrillation (AF) is a common heart disease and it is estimated to be present in 1% to 2% of the general population [9]. AF and hypertension commonly coexist [9]. Thus, AF's effects on the PTT-BP model should be critically considered when performing PTT-based on BP estimation on hypertensive patients. To find Impact of AF on the PTT and BP, and validate the capability of PTT based cuff-less BP estimation methods on AF patients, the present study investigates PTT and BP relationship in AF patients and compared their PTT variations between AF and non-AF status. Additionally, two most cited cuff-less BP estimation methods

Research supported by the National Key Research and Development Program of China (2018YFC1312000). the National Natural Science Foundation of China (61801145), and the Basic Research Project of Shenzhen Science and Technology Program (JCYJ20180306171800589).

1 Department of Electronic and Information Engineering, Harbin Institute of Technology at Shenzhen, Shenzhen, Guangdong, China.
2 Advanced Innovation Center for Human Brain Protection, Capital Medical University, Beijing, China.
3 National Clinical Research Center for Geriatric Disorders, Xuanwu Hospital, Capital Medical University, Beijing, China.
4 Peng Cheng Laboratory, Shenzhen, Guangdong, China.
*Corresponding author: Ting Ma. Phone: +86-755-26033608; fax: +86- 755-26033608; email: tmahit@outlook.com.

were performed on these patients to investigate the Impact of AF on the accuracy of PTT based cuff-less BP estimation.

II. Materials and Methods

A. Data

We selected the open source critical care waveform database, MIMIC III database matched subset as the data source in our study[10, 11]. This database contains waveform records matched with MIMIC III clinical database, which allows us to analyze the waveform records based on clinical information. In this study, we randomly selected 200 patients whose electrocardiogram (ECG), arterial blood pressure (ABP), and photoplethysmography (PPG) waveform were simultaneously recorded.

AF usually coexists with many diseases which may potentially influence the waveform data. To avoid those potential artifacts, we only selected data when patients did not suffer adverse clinical events like hypotension, shock, or sepsis. Also, all patients must not have received any clinical interventions and drug therapies during the selected period and their mean arterial pressure (MAP) must be larger than 70 mmHg. Finally, 60 minutes long waveform records were extracted from each selected patient, and totally 200 hours long clinical waveforms (ECG, ABP and PPG) were involved in the study.

B. Atrial Fibrillation Identification

AF is characterized by arrhythmia and the onset of AF could continue from few seconds to few hours. To our best knowledge, there is no golden standard for AF diagnosis. In this study, a supervised machine learning framework was proposed to deal with the identification of AF. Because there is no AF label in the MIMIC data, we first used the MIT-BIH atrial fibrillation database [12]to develop our identification model, and then deployed the model in the MIMIC III database.

The MIT-BIH atrial fibrillation database includes twenty-five long-term ECG recordings of human subjects with AF. For each recording, heartbeats and the exact onset time of AF was annotated by experienced physicians. These experts labeled data can be used as the ground truth when training the machine learning framework. In our model, the ECG recording was first split into 30 seconds long data frame and then these data frames were manually classified as AF or normal according to the annotation. After data classification, five feature metrics – mean, standard derivation, sample entropy, quadratic entropy and coefficient of sample entropy of R-R intervals were computed for each data frames [13, 14]. A logistic regression model was finally constructed to produce a probability of being AF for each data frame. The details of this machine learning framework are shown in Fig.1.

The proposed AF identification model could achieve a receiver operating characteristic (ROC) area under the curve (AUC) performance of 0.99 with leave-one-subject out cross validation, meaning it could discriminate AF very well in the MIT-BIH database. The AF identification model was finally deployed in our selected MIMIC III data. The selected MIMIC III data was first split into 30s long data frame and its feature metrics of R-R interval was computed. The features metrics of each data frame was input into the identification model to get the probability of being AF.

To discriminate AF data frames in the selected MIMIC III waveforms, we used the probability computed by the AF identification model as the criteria to discriminate AF. In order to get solid AF and normal physiological data, data frames with probability larger than 0.7 were labeled as AF, and data frames with probability less than 0.2 were labeled as normal. Only patients who have both AF and normal data frames would be finally involved. Finally, 74 patients with 2372 AF data frames and 3051 normal data frames were involved.

C. PTT Computation and BP Estimation

In the present study, the pulse transit time (PTT) was defined as the time interval between the ECG R wave peak and the PPG waveform foot during the same cardiac cycle. Besides PTT, PPG graphic feature, the Photoplethysmography Intensity Ratio (PIR) were also computed for the BP estimation. Other important physiological parameters include R-R intervals were extracted from the ECG R-R peak, and the systolic blood pressure (SBP), diastolic blood pressure (DBP) were also computed from the ABP waveform as the reference BP value.

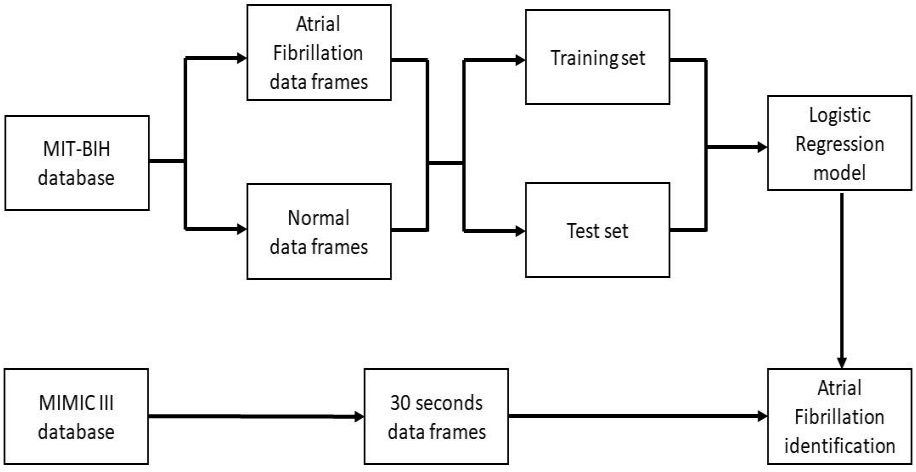

Fig.1 Data flow of Atrial Fibrillation Identification Framework

Two most cited BP estimation methods were involved in this study, there are 1) PIR based BP estimation [15], and 2) BP estimation using solely PTT [16]. For the PIR based method, the BP was calculated using (3) and (4).

$$DBP = DBP_0 * \frac{PIR_0}{PIR} \quad (3)$$

$$SBP = DBP + (SBP_0 - DBP_0) * \left(\frac{PTT_0}{PTT}\right)^2 \quad (4)$$

DBP_0, PIR_0, and PTT_0 are the calibration value of DBP, PIR, and PTT. PIR is the ratio of PPG peak intensity and PPG foot intensity. This method uses both PTT and PPG graphic features. The other BP estimation method using solely PTT, the BP was calculated using equation (5) and (6).

$$DBP = \frac{1}{3}SBP_0 + \frac{2}{3}DBP_0 + \frac{2}{\gamma}\ln\frac{PTT_0}{PTT} - \frac{SBP_0 - DBP_0}{3} * \left(\frac{PTT_0}{PTT}\right)^2 \quad (5)$$

$$SBP = DBP + (SBP_0 - DBP_0) * (\frac{PTT_0}{PTT})^2 \quad (6)$$

γ is a constant coefficient related to the arterial wall elasticity, in this study, γ is equal to 0.031mmHg^{-1} [17].

In order to measure these two methods' abilities in tracking the BP for AF patients, the difference mean and standard derivation (STD) between estimation BP and reference BP were used as evaluation. Student t-test were also performed to investigate the differences between AF and normal groups.

III. RESULTS

A. Univariate Analysis of PTT and BP

We first performed a univariate analysis on PTT, PIR and BP. Table I shows the value of these parameters. It is investigated that, the R-R interval of AF data frames is 723.75±314.29 ms, where it is significantly different ($p<0.01$) from the value of normal data frames (858.68±146.74 ms). This result is in correspondence with our common knowledge that AF is characterized by the arrhythmia, indicating a changed and varied R-R interval. Data frames with AF have a shorter mean R-R interval but with larger variations comparing to the normal data frames, demonstrating the ability of our proposed model to identify the AF. Besides the R-R interval, the pulse interval also shares the similar variations with the R-R interval that its standard derivation in AF data frames is larger than the value in normal data frames. All these results indicate that AF not only influence the heart rhythm, but would also impact the arterial pulse rhythm.

TABLE I. UNIVARIATE ANALYSIS OF PARAMETERS

Parameter name	*AF*	*Normal*	*P-value*
R-R Interval (ms)	723.75±314.29	858.68±146.74	<0.01
Pluse Interval (ms)	776.42±414.07	869.43±355.25	<0.01
Pulse transit time (ms)	397.81±153.87	419.42±123.63	<0.01
PRI(1)	1.21±11.82	1.01±10.51	0.18
Systolic blood pressure (mmHg)	105.67±19.35	105.95±20.34	0.06
Diastolic blood pressure (mmHg)	50.20±8.71	51.13±9.38	<0.01

TABLE II BP ESTIMATION ERROR

Method	*AF (mmHg)*	*Normal (mmHg)*	*P-value*
Method1–SBP	1.79±26.93	0.45±21.51	<0.01
Method1-DBP	0.14±12.41	0.03±9.07	<0.01
Method2-SBP	3.62±28.68	0.74±22.79	<0.01
Method2-DBP	4.23±16.12	2.11±10.93	<0.01

The PTT value in AF data frames is 379.81±153.87 ms, where the PTT value of normal data frames is 419.42±123.63. AF data frames have a smaller but more varied PTT than the normal data frames. But no significant differences were found in the PIR value between AF and normal data, the PIR value of AF group is 1.21±1.82, where the PIR of normal group is 1.01±1.51. When we investigate the SBP, there is no significant differences between AF (105.67±19.35 mmHg) and normal group (105.95±20.34 mmHg), but weak significances were found in the DBP, DBP of AF group (50.20±8.71mmHg) is little lower than the value in normal group (51.13±9.38 mmHg).

B. BP estimation results

Two different BP estimation method were performed in this study to investigate their performances in AF patients. The first method, which call method1, use both PPG graphic features and PTT to predict the BP value. The second method use solely PTT to predict the BP, call methods. Their results were shown in Table II. Significant differences were investigated in the estimation results between AF and normal groups. For the method1, the estimation error of SBP in AF patients is 1.79±26.93 mmHg, higher than the error in normal group (0.45±21.51 mmHg); similar results were also investigated when estimating the DBP (0.14±12.41 mmHg in AF patients and 0.03±9.07 mmHg in normal group). For the method2, the accuracy of BP estimation for the AF patients are also worse than the accuracy for normal subjects.

IV. DISCUSSION

In this study, we investigated 74 randomly selected critically ill patient to see whether AF would influence the PTT value and BP. The preliminary results showed that patients would have a more varied PTT and more complex beat to beat PTT sequence when AF onset, indicating the AF would impact both heart rhythm and pulse rhythm. Further performing PTT based BP estimation algorithm on the data shows that the onset of AF would decrease the estimation accuracy. but PPG graphic feature, the PIR would not be influenced by AF, and PIR is still a predictive factor for the BP estimation even though the patient has arrhythmia disease like AF.

AF is a common sustained cardiac arrhythmia, it is characterized by rapid and irregular heartbeats and coexists with decreasing cardiac output. This is in correspondence with our preliminary results that the mean R-R interval and pulse interval were decreased but their variation increased when AF

occurs. It is also hypothesized that AF would simultaneously affect the heart rhythm and the pulse rhythm. Data in Table. I shows that AF would increase the pulse interval variation. Further analysis on the beat to beat SBP and DBP value demonstrate that the BP value would not vary too much when the AF occurs. There is no significant difference of SBP between AF and normal groups, but significant differences were found in DBP. We hypothesized that it is because when AF occurs, even the irregular heart rhythm would also influence the left ventricle ejection volume, resulting the decreased stroke volume and decreased DBP.

AF would influence the patients' cardiac function, resulting in the changed heart rhythm, pulse rhythm, cardiac output, etc., thus influence the PTT value. In our results, significant differences were found in the PTT value between AF and normal group. But the other PPG derived feature, the PIR, remains stable when AF occurs. PIR refers to the arterial vasomotion. We hypothesized that it is because the AF would only impact the cardiac function but patient's vascular functions remain stable, thus patients' PIR value does not changed.

Further investigation on the BP estimation results shows that, the accuracy of BP estimation algorithm would significantly decrease on the AF data comparing to the normal data. And the performances of BP estimation method using solely PTT is worse than the method using PTT and PIR. The estimation results on DBP is better than the results on SBP. We think it is because the PTT values significantly goes down when AF occurs, but patient's BP level remain stable in total, causing the inaccuracy of PTT based BP estimation. For the PIR based BP estimation, it is investigated that because the PIR value remain stable, the difference of BP estimation accuracy between AF and normal groups is smaller than other PTT based method. PIR is still a good predictor for the BP estimation.

There are still many limitations in this study. First, the research subjects involved in our study are critically ill patients, meaning that there are potentially other diseases would influence our study. Second, the finding in our study is based on the paired comparison between AF status and normal status in critically ill patients, where no healthy people were involved. Our future research would focus on the mechanisms of cuff-less BP estimation models in cardiac disease patient, and aim to improve the performance of BP estimation on those patients.

V. Conclusion

In this study, we validated current BP estimation model on AF patients. Our preliminary results find that AF would not influence the patient's BP values, but would significantly increase the variations of PTT. PIR as a PPG graphic features is not influenced by AF. Further investigation on the BP estimation show that the AF would decrease the BP estimation accuracy, but accuracy of PIR based BP estimation is better than the PTT based method. This study therefore demonstrates that AF would impact the PTT-BP relationship, but the PIR is still a good predictor of BP in AF patients.

Acknowledgment

This study was supported by the National Key Research and Development Program of China (2018YFC1312000). the National Natural Science Foundation of China (61801145), and the Basic Research Project of Shenzhen Science and Technology Program (JCYJ20180306171800589).

References

[1] S. I. Hay et al., "GBD 2015 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015 (vol 388, pg 1659, 2016)," Lancet, vol. 389, no. 10064, pp. E1-E1, Jan 7 2017.

[2] C. K. Chow et al., "Prevalence, awareness, treatment, and control of hypertension in rural and urban communities in high-, middle-, and low-income countries," Jama, vol. 310, no. 9, pp. 959-968, 2013.

[3] Y. Chen, C. Wen, G. Tao, M. Bi, and G. Li, "Continuous and noninvasive blood pressure measurement: a novel modeling methodology of the relationship between blood pressure and pulse wave velocity," Annals of biomedical engineering, vol. 37, no. 11, pp. 2222-2233, 2009.

[4] Y. Chen, S. Shi, Y. K. Liu, S. L. Huang, and T. Ma, "Cuffless blood-pressure estimation method using a heart-rate variability-derived parameter," Physiological Measurement, vol. 39, no. 9, Sep 2018.

[5] R. Mukkamala et al., "Toward Ubiquitous Blood Pressure Monitoring via Pulse Transit Time: Theory and Practice," IEEE Transactions on Biomedical Engineering, vol. 62, no. 8, pp. 1879-1901, 2015.

[6] X. R. Ding, Y. T. Zhang, and H. K. Tsang, "Impact of heart disease and calibration interval on accuracy of pulse transit time–based blood pressure estimation," Physiological Measurement, vol. 37, no. 2, p. 227, 2016.

[7] D. R. Wagner et al., "Relationship between pulse transit time and blood pressure is impaired in patients with chronic heart failure," Clinical Research in Cardiology, vol. 99, no. 10, pp. 657-664, Oct 2010.

[8] J. Spiesshofer et al., "Validation of blood pressure monitoring using pulse transit time in heart failure patients with Cheyne-Stokes respiration undergoing adaptive servoventilation therapy," Sleep and Breathing, vol. 18, no. 2, pp. 411-421, May 2014.

[9] A. J. Manolis et al., "Hypertension and atrial fibrillation: diagnostic approach, prevention and treatment. Position paper of the Working Group 'Hypertension Arrhythmias and hrombosis' of the European Society of Hypertension," Journal of Hypertension, vol. 30, no. 2, pp. 239-252, Feb 2012.

[10] A. E. W. Johnson et al., "MIMIC-III, a freely accessible critical care database," Scientific Data, Data Descriptor vol. 3, p. 160035, 05/24/online 2016.

[11] A. L. Goldberger et al., "PhysioBank, PhysioToolkit, and PhysioNet," Components of a New Research Resource for Complex Physiologic Signals, vol. 101, no. 23, pp. e215-e220, 2000.

[12] G. Moody, "A new method for detecting atrial fibrillation using R-R intervals," Computers in Cardiology, pp. 227-230, 1983 1983.

[13] D. E. Lake and J. R. Moorman, "Accurate estimation of entropy in very short physiological time series: the problem of atrial fibrillation detection in implanted ventricular devices," American Journal of Physiology-Heart and Circulatory Physiology, vol. 300, no. 1, pp. H319-H325, Jan 2011.

[14] M. Carrara et al., "Heart rate dynamics distinguish among atrial fibrillation, normal sinus rhythm and sinus rhythm with frequent ectopy," Physiological Measurement, vol. 36, no. 9, pp. 1873-1888, Sep 2015.

[15] X. R. Ding, Y. T. Zhang, J. Liu, W. X. Dai, and H. K. Tsang, "Continuous Cuffless Blood Pressure Estimation Using Pulse Transit Time and Photoplethysmogram Intensity Ratio," IEEE Transactions on Biomedical Engineering, vol. 63, no. 5, pp. 964-972, 2016.

[16] Y. Zheng, "Unobtrusive Cuff-less Arterial Blood Pressure Measurement and Cardiovascular Risk Evaluation," The Chinese University of Hong Kong (Hong Kong), 2014.

[17] A. J. Bank, R. F. Wilson, S. H. Kubo, J. E. Holte, and H. Wang, "Direct Effects of Smooth Muscle Relaxation and Contraction on In Vivo Human Brachial Artery Elastic Properties," Circulation Research, vol. 77, no. 5, pp. 1008-1016, 1995.