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Development of Evaluation System Using Photoplethysmography Sensors for Intradialytic Hypotension Monitoring

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Complications of hemodialysis (HD) treatment include hypotension, hypertension, imbalance syndrome, and chest pain. The incidence of hypotension ranges from 25 to 50%, making it as the most common complication during HD. Repeated hypotension causes blood stagnation and leads to excessive heart workload of patients. Moreover, clinical studies proposed that the incidence of hypotension has a high correlation with the rate of mortality. In clinical practice, blood pressure (BP) measurement by nursing staff every 30 to 60 min or the patient claiming of discomfort is required to detect intradialytic hypotension (IDH). In this study, we developed an evaluation system using photoplethysmography (PPG) sensors for IDH monitoring. The system acquired heart rate variability (HRV) from PPG sensors and arterial pressure (AP) from dialysis machines to provide an immediate classification of IDH risk. We divided IDH patients into three classes from low to high risk, with the third category having the highest risk. To verify the accuracy of the system, we designed a clinical trial to compare measurements obtained with the system with BP measurements taken by clinical staff. The results from 12 patients indicated that the accuracy of the proposed system was 90%, indicating its high potential to provide a simple and fast assistance system for assisting in the clinical evaluation of IDH.

1. Introduction

Intradialytic hypotension (IDH) is a common clinical complication, and research statistics show that up to one-third of hemodialysis (HD) patients have experienced hypotension during

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dialysis treatment.[1] In some patients, the development of hypotension necessitates intravenous fluid replacement before they are able to safely leave the dialysis unit. IDH may reduce the efficacy of dialysis and contribute to the excessive morbidity and mortality associated with HD. There is roughly a 15–30% probability that hypotension occurs during HD, and repeated hypotension causes blood stagnation and leads to excessive heart workload of patients. We can also predict the morbidity and mortality of cardiovascular disease from this parameter of hypotension. Moreover, the blood flow rate and heart rate (HR) change with the patients' blood pressure (BP). Many previous studies focused on the reasons for hypotension in HD, which included a study of the parameters that can help predict hypotension. The research results show that there is a correlation between BP variability (BPV) and abnormal HR variability (HRV).[1–4]

A previous study proposed that hypotension during HD may be caused by the activation of a cardiovascular reflex causing abrupt sympathetic withdrawal, vasodilation, and bradycardia (bradycardic hypotension).[3] To assess the prevalence of bradycardic hypotension and test the hypothesis that dialysis patients are predisposed to vasodepressor syncope, a study was performed to determine the relationship between HRV and BP changes. The results show that patients developing bradycardic hypotension all had an erratic HR response to hypotension (i.e., bradycardia preceded or followed by tachycardia or by no HR change) and were characterized either by the typical hemodynamic pattern of hypovolemia (predialysis hypotension, tachycardia, and low total body water) or by treatment with a very high ultrafiltration rate (>0.3 ml/kg/min). They concluded that tachycardia was the more frequent HR response to dialysis hypotension in uremic patients. Bradycardic hypotension in dialysis patients has been associated with a hemodynamic profile indicating a more severe cardiovascular system. Bradycardic hypotension probably represents a physiological response to hypovolemia rather than the expression of a peculiar predisposition to vasodepressor syncope.[3] In 2016, Chang *et al.* conducted a clinical trial assessing hypotension and HRV during HD.[4] There were 111 patients recruited in that study, and their HRV was measured before and between HD sessions. The results of the study show a correlation between HRV and dialysis-induced hypotension.

Dialysis machines can provide many biological details of patients; hence, some studies have focused on the analysis of biological information, such as arterial pressure (AP). In 2015, Holmer *et al.* noted that although patients undergoing HD treatment often suffer from cardiovascular disease, cardiac rhythm is not monitored on a routine basis, and the signal monitored is mainly the AP signal from the dialysis machine.[5] They proposed a method of extracting a cardiac signal from the built-in extracorporeal venous pressure sensor of an HD machine without requiring an extra sensor. A difficulty in extracting the cardiac signal is that the cardiac component is much weaker than the pressure component generated by the peristaltic blood pump in the dialysis machine. To further complicate the extraction problem, the cardiac component is difficult to separate when the pump and heart beats coincide. In this study, they estimated HR by subtracting an iteratively refined blood pump model with an AP signal and comparing it with a photoplethysmography (PPG) reference signal, resulting in a difference of 0.07 ± 0.84 beats/min. The accuracy was sufficient for the analysis of HR and certain cardiac arrhythmias.[5]

An AP signal displayed on a dialysis machine is susceptible to other factors, such as fistula stenosis or the adjustment of the speed of dialysis at that time; hence, many studies have used other methods of detecting the degree of fistula stenosis[6,7] and attempted to rapidly detect the degree of fistula stenosis and reduce the risk of dialysis. As mentioned above, even though both AP and HRV are parameters highly correlated with IDH, currently there is no tool that can directly use these two parameters to evaluate IDH. Therefore, clinicians only rely on the BP taken by nursing staff every 30 to 60 min or complaints of patient discomfort to detect IDH, which requires too much clinical human resources. In accordance with the above literature, we developed an evaluation system for AP and HRV using a PPG sensor, which is often used to measure HRV along with noninvasive sensors for different IDH risks. We also compared the measurements obtained by the newly developed system with BP measurements taken by clinical staff to discuss the accuracy and the relationship between these parameters.

2. Materials and Methods

2.1 Data analysis architecture

We proposed a system that assists caregivers in interpreting the risk of hypotension in patients during dialysis through AP and HRV signals. First, three signals are obtained: (a) the patient's pulse pressure signal captured by the transmission control protocol (TCP) and internet protocol (IP) from a dialysis machine (NCU-18, NIPRO, Japan); (b) the patient's PPG signal measured by a biofeedback system (ProComp5 Infiniti™ T7525, Thought Technology, Canada) and transmitted it through Bluetooth; (c) the patient's BP signal measured by a device (CSI-506W3, Criticare, USA) and by medical staff at regular time periods. Subsequently, all three signals are integrated by the proposed system for classification and statistical analysis, and then the analyzed data is displayed on the screen interface. A flowchart of the whole process is shown in Fig. 1.

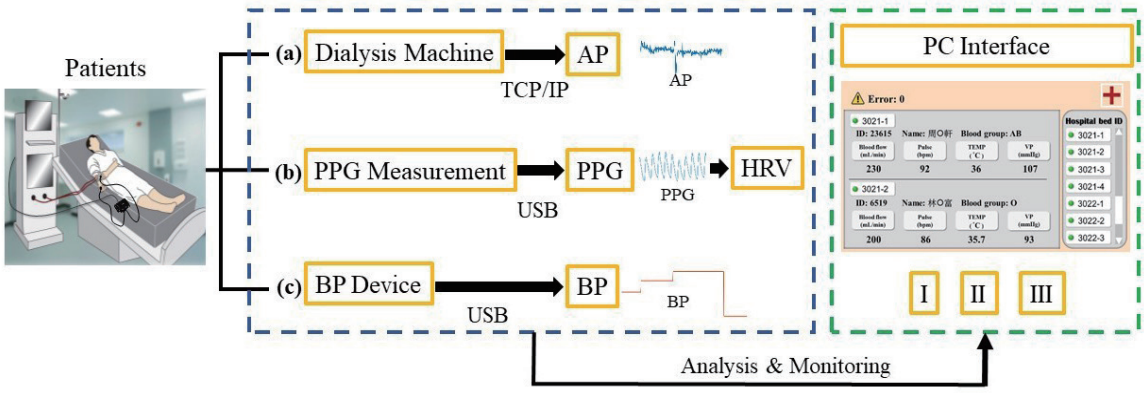


Fig. 1. (Color online) Signal processing of the proposed system.

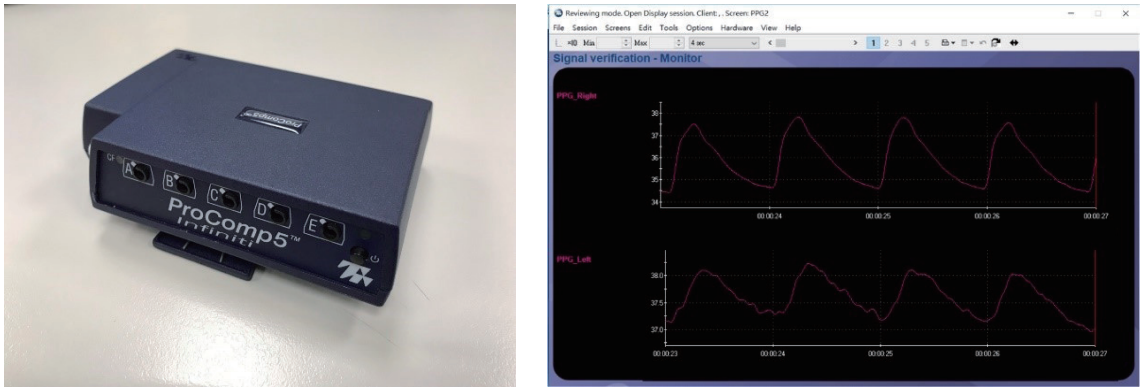
2.1.1 AP measurement

We aimed to develop a rapid and reliable initial evaluation system. To obtain data of uremic patients during an HD session, we used a dialysis machine with a 100–800 mL/min dialysis flow range, which can provide multiple information, including venous pressure, dialysate pressure, blood flow rate, AP, and BP.[8] In addition, the dialysis machine can receive computer orders via TCP/IP technology and transmit the information of dialysis patients to the host computer.

2.1.2 PPG measurement

To obtain reliable and stable PPG signals, we used a computerized biofeedback system to measure the PPG signals of uremic patients during HD sessions. The biofeedback system is housed in an ergonomically designed case and can capture real-time data through its connection to a PC via its fiber-optic cable or Bluetooth.[9] There are five channels in this sensor; the first two channels provide 2048 sample rates for viewing raw data including PPG, electroencephalography, surface electromyography, electrocardiography, and HR/BVP signals, and the remaining three channels provide 256 sample rates for slower signals such as respiration, temperature, and force. In addition, using "BioGraph Infiniti" software (Fig. 2), a real-time display of the signals is available on the PC, and functions such as channel settings, interface changes, and data outputs can be adjusted.

In this study, PPG measurement in the biofeedback system used a blood volume pulse (BVP) sensor, which can also help with the real-time identification and diagnosis of IDH to analyze the PPG signal. BVP is used for measuring the amount of infrared light reflected from a skin surface, which varies with the amount of blood in the skin. Every heartbeat (pulse) brings more blood into the skin, which reflects red light and absorbs other colors. The BVP signal is a relative measurement, so there is no standard unit, but it can be used for HRV calculation. In addition, the deviation of the amplitude could be useful information for clinical applications.



(a) (b)

Fig. 2. (Color online) (a) Thought Technology ProComp 5 Infiniti T7525-5 channel encoder and (b) BioGraph Infiniti software interface.[9]

2.1.3 Classification of IDH

We followed the classifications in the literature,[9] including the definitions in the Kidney Disease Outcomes Quality Initiative (KDOQI) and European Best Practice Guidelines. In this study, the risk of IDH was classified as shown in Fig. 3. When the systolic BP (SBP) of a uremic patient was below 100 mmHg or there was a decrease in SBP of at least 20 mmHg, the patient was classified into Class III. When IDH was detected as a decrease in SBP of at least 10 mmHg but no related IDH symptoms were found, the patient was classified into Class I group. A patient having IDH-related symptoms and a decrease in SBP of at least 10 mmHg was classified into Class II. In addition, we used the pNN50 index (percentage of successive RR intervals that differ by more than 50 ms) to estimate the number of HRV variants in IDH,[7] and by applying the same concept, the number of abnormal APs was calculated with a threshold variation of 5% as an input for the subsequent real-time classification.

2.2 Subjects

In this study, 12 subjects with average age and standard deviation (SD) of 61.8 ± 7.4 (47 to 70 years) were recruited from the Institutional Review Board (IRB No. VGHKS19-CT5-04) of Kaohsiung Veterans General Hospital (KVGH), Tainan Branch. Subjects were scheduled in the order in which they signed up to participate in this study. Details and inclusion criteria are shown in Table 1.

After the fistula was completed, the patients were instructed to take care of the AVF during the first six to eight weeks after surgery. This was to avoid damaging the new fistula so that

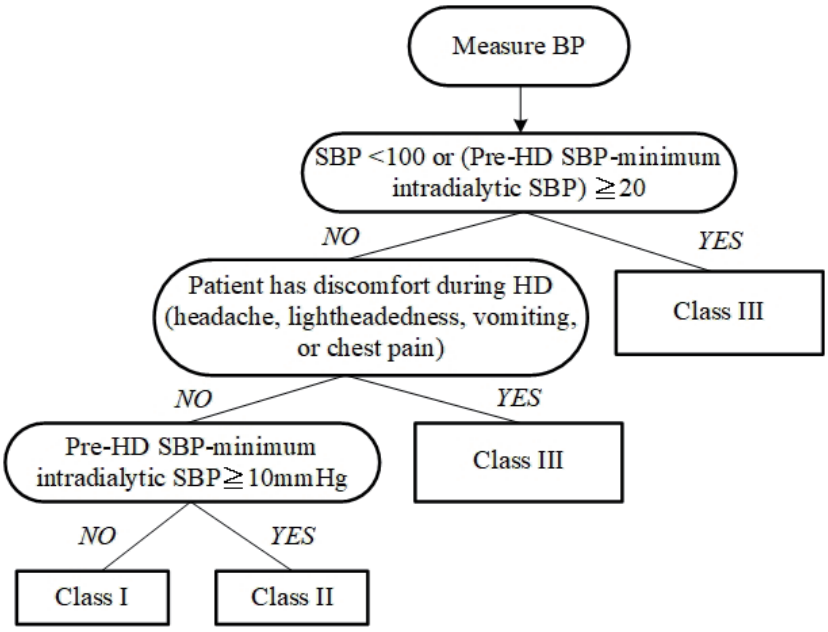


Fig. 3. Flowchart of risk classification of IDH.

Table 1
Inclusion criteria.

	Male	Female	Inclusion criteria
No. of subjects	9	3	• Had signed the consent • Age between 20 and 70 years old
Average age	64.7	53	• Arteriovenous fistula (AVF) was created after 8 weeks and arteriovenous graft (AVG) after 6 weeks • No history of arrhythmia or in agitation
Age SD	4.5	7.9	• No restlessness • No traumatic wound or risk of infection in fistula

HD could be performed effectively and to increase blood circulation and allow the intima to mature in the fistula, enabling the venous wall to withstand repeated dialysis punctures. The period of six to eight weeks is a key determinant of whether the dialysis can be performed smoothly in the future. In addition, patients over 70 years old are usually not stable, having multiple chronic diseases; therefore, we classified the above criteria as priority exclusions in subject selection. When the HD treatment started, we monitored the patient's PPG signal with the biofeedback system by attaching its sensor to the patient's index finger. At the same time, we connected the dialysis machine to read parameter information of the patients and recorded their clinical data periodically. Figure 4 is a flowchart of managing the clinical data in the terminal computer.

3. Results

To verify the stability of the system and the accuracy of hypotension assessment through AP in dialysis, a series of experiments were performed.

3.1 IDH classification by HRV and AP

According to the results of HRV analysis, we established a classification rule of IDH. The classification results had an accuracy of 85% in evaluating IDH by only HRV.

During the HD session, PPG signals were measured sequentially and combined with the dialysis machine to detect BP signals. We segmented the signals into 40 pieces of data according to the measurement time of the patient's BP by nursing staff. The average and SD of HRV for the different classes of IDH were 7.3 ± 3.4 in Class I, 25.6 ± 3.8 in Class II, and 40.1 ± 8.4 in Class III as shown in Fig. 5. There was a significant between-group difference in the number of abnormal HRV in our IDH risk classification ($p < 0.01$).

As shown in Fig. 6, the average and SD of AP in the different classes of IDH were 7.8 ± 6.1 in Class I, 26.5 ± 5.2 in Class II, and 40.8 ± 9.1 in Class III. There was a significant between-group difference in the number of abnormal AP in our IDH risk classification ($p < 0.01$).

According to the analysis of the frequency of abnormal AP, we established a rule for classifying IDH. This classification results had an accuracy of 80% in evaluating IDH by only AP.

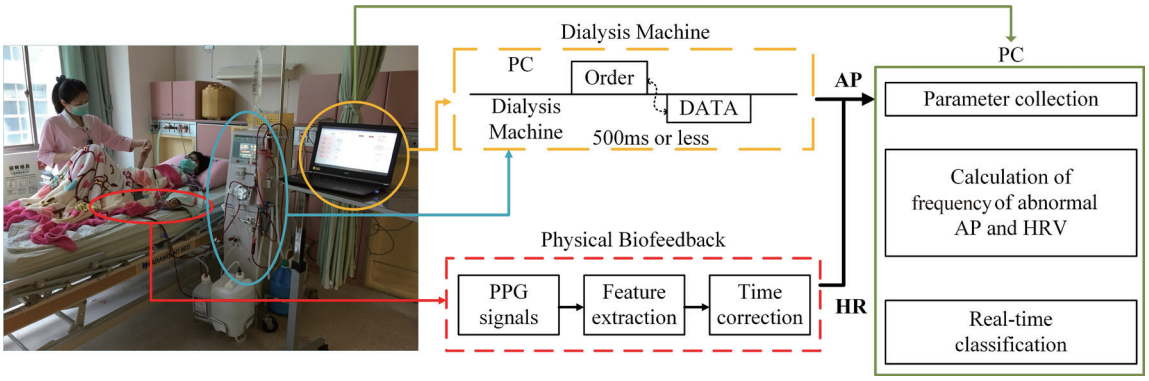


Fig. 4. (Color online) Flowchart of management of clinical data in the computer.

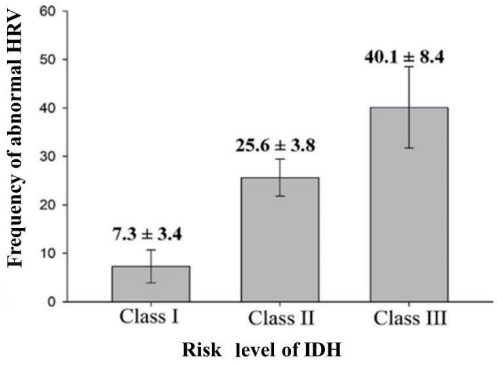


Fig. 5. Relationship between HRV and IDH class.

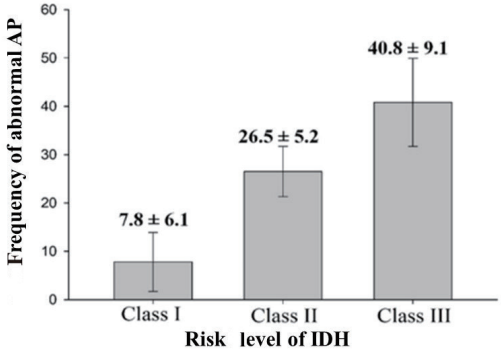


Fig. 6. Relationship between AP and IDH class.

3.2 Proposed model of HRV and AP for IDH classification

To increase the accuracy of IDH evaluation, we combined two parameters, AP and HRV, for IDH classification to evaluate the risk of IDH. We classified patients having AP below 13 into Class I, patients with HRV above 30 into Class III, and other patients into Class II. Subsequently, we introduced clinical data from 12 patients into the classification rule, and the results are shown in Fig. 7. Among the 40 pieces of data, four records were incorrectly assigned. The first two incorrectly classified pieces of data should be Class I, as determined by clinical BP, but were classified as Class II by the classification rules in this study; the other two pieces of data should be Class II but were classified as Class III. As a whole, the overall accuracy was 90%, as shown in Table 2.

To explore the causes of the inappropriate classification of the four data, we performed an ultrasound study of the subjects' A-V fistula to detect their stenosis levels. By ultrasonic imaging, we found that, in these patients, there was more than one site of stenosis in A-V fistulae. This resulted in different APs in the same A-V fistula and inappropriate data in the classification. Thus, the risk of IDH can be classified accurately by using HRV and AP combined with the simple classification rule. However, a multiple-site condition reduced the classification accuracy.

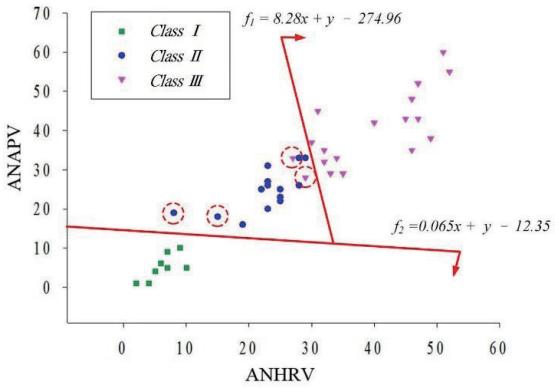


Fig. 7. (Color online) Results of analysis with classification rule using AP and HRV. (Circles indicate inappropriately classified data).

Table 2
Analysis results obtained using HRV and AP in evaluation of IDH risk.

	Class I	Class II	Class III	Accuracy (%)
G/R	10/8	14/14	16/18	90

*G: ground truth, R: results of classification

4. Discussion and Conclusion

Currently, the monitoring of the BP change of uremic patients during an HD session depends on measurements performed by nursing staff at regular intervals. Previous clinical studies revealed that the incidence of IDH had a high correlation with mortality due to HRV, making it a good factor for evaluating IDH risk. On the other hand, AP data from a dialysis machine can be detected easily. According to previous research, the accuracies of support vector machine (SVM) and logistic regression analysis (LRA) for IDH are 81.3 and 76.3%, respectively. In this study, we combined AP and HRV obtained from PPG sensors to effectively predict three categories of IDH risk, and the accuracy reached 90% in real-time classification, which is a significant improvement compared with past studies. The results also indicate that the proposed system with PPG sensors has high potential as an assistant clinical tool for the evaluation of IDH. However, some issues should be resolved for future clinical application. For example, the wearable devices were easily affected by patients' movement during HD, and some dialysis machines may not be able to provide output signals of AP. Additionally, to verify the results of this study, further clinical trials to collect more data and system tests are necessary.

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