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Changes in the spectral powers of finger photoplethysmographic waveform variability in hemodialysis patients

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Abstract— **This paper reports changes in the spectral powers of finger photoplethysmographic waveform variability (PPGV) following hemodialysis compared to pre-dialysis. The results are based on data collected from 12 hemodynamically stable patients having regular hemodialysis thrice weekly. Six minutes of continuous electrocardiogram (ECG) and finger infra-red photoplethysmographic (PPG) signals were collected at pre-dialysis and at end of dialysis. A four minute artefact free segment was selected and baseline and amplitude variabilities were derived from PPG waveform. Heart rate variability was derived from ECG R-R interval. Frequency spectrum analysis was then applied to these variability signals. The spectral powers were then calculated from low frequency (LF), mid frequency (MF) and high frequency (HF) bands. The results indicate that LF ($p = 0.01$) and MF ($p = 0.02$) powers of baseline PPGV (expressed in mean-scaled units) and LF ($p = 0.006$), MF ($p = 0.003$) and HF ($p = 0.017$) powers of amplitude PPGV (expressed in mean-scaled units) showed a significant increase at the end of dialysis compared to pre-dialysis. HRV spectral measures did not show any significant change. The increase in LF and MF powers in PPGV may suggest the recovery and further enhancement of peripheral sympathetic vascular modulation as a result of volume unloading in initially hypervolemic dialysis patients, at the same time the increase in respiratory HF power in PPGV may indicate preload reduction.**

I. INTRODUCTION

Loss of renal function often leads to accumulation of excess blood volume in the end-stage renal failure patients. Peripheral vasodilation serves as a major compensatory mechanism which is probably affected by uremia secondary to chronic renal failure [1], [2], [3]. Hemodialysis serves as an important therapy to remove excess body fluid (through blood ultrafiltration). Augmentation of sympathetic nervous system activation of peripheral vasoconstriction and modest heart rate increase serve as normal compensatory responses to central hypovolemia in order to increase cardiac output and maintain blood pressure [2], [3].

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The spectral analysis of heart rate variability (HRV) has long been used as a tool to assess the changes in the autonomic nervous system activity during dialysis. The power spectrum of HRV has been divided into a low frequency (LF) band and a high frequency (HF) band. The LF band is influenced by both sympathetic and vagal nerve activity whereas the HF band predominantly reflects respiratory vagal modulation of heart rate [4], [5]. In dialysis sessions uncomplicated by hypotension, the LF power has been observed to increase relative to HF power, which may be interpreted as both deactivation of vagal nerve influence and activation of sympathetic nervous system influence [6], [7].

The variability of finger photoplethysmographic (PPG) waveform can be used to monitor the sympathetic control of peripheral vasculature [8], [9], [10], [11]. The power spectrum of PPGV can be divided into a LF band that is believed to reflect sympathetic-related vascular activity with minimal direct vagal influence, and a HF band that is governed by the mechanical effect of respiration on venous return [8]. A portion of LF band termed as mid frequency (MF) band is considered as a more specific marker of sympathetic vascular modulation within autonomic reflex mechanisms [4], [9]. Previous studies have suggested that the presence and relative strength of spontaneous LF waves in finger PPGV may indicate the degree of sympathetic control over peripheral circulation [8], [9], [10], [11]. The strength of respiratory variation in PPGV, which governs HF power, may increase with preload reduction [10], [12], [13], [14].

Baroreflex dysfunction and withdrawal of reflex vasoconstriction are two important factors resulting in hemodialysis-induced hypotension, with the latter considered more sensitive [2]. We believe that ability to non-invasively monitor autonomic activity during dialysis may have enormous potential benefits in the early identification of intradialytic hypotension. This paper utilizes the spectral measures of PPGV to investigate the changes in the peripheral circulatory response to hemodialysis. The results show that that fluid removal during stable hemodialysis, leads to increase in PPGV LF and MF spectral powers due to enhanced sympathetic activation of peripheral vasculature leading to systemic vasoconstriction; and increase in PPGV HF spectral power due to preload reduction. To our knowledge this is the first study to evaluate the changes in spectral measures of finger PPGV during hemodialysis. The study was based on comparison of spectral powers of PPGV between pre-dialysis and end of dialysis. Future studies are required to observe these changes throughout dialysis.

TABLE I
PATIENT CHARACTERISTICS

Characteristics	Values
N	12
Age(yrs)	67 $\pm$ 3
Height (cm)	165.3 $\pm$ 3.2
Length of time on Dialysis (months)	12.8 $\pm$ 4.7
Dialysis Duration (hrs)	4.36 $\pm$ 0.2
Pre-Dialysis Weight (Kgs)	84.6 $\pm$ 5.7
Post-dialysis Weight (Kgs)	81.9 $\pm$ 5.5
Fluid Removed (Litre)	3.1 $\pm$ 0.35

II. MATERIALS AND METHODS

A. Subjects

A group of 12 end-stage renal failure patients having regular hemodialysis at the Hemodialysis Unit, Prince of Wales Hospital, Sydney, Australia were enrolled in this study. All patients were hemodynamically stable with no prior symptoms of intra-dialytic hypotension, and were routinely dialyzed three times weekly for 4-5 hours. All patients were dialyzed using an AK200S or AK200 Ultra S (Gambro, Lund, Sweden) machine. Dialysis was performed using the Polyflux 210H (Gambro, Lund, Sweden) dialyzer with blood flow rate ranging from 300-350 ml/min, dialysate flow rate of 500 ml/min; and the dialysate temperature set to 36^oC. The treating physician varied the dialysate fluid composition according to individual prescription. The ultrafiltration rate was set based on the amount of fluid to be removed, as was the dialysis duration. Clinical characteristics of included patients are tabulated in Table I. The study was reviewed and approved by the Human Research Ethics Committee of the Prince of Wales Hospital, Sydney and informed consent was obtained from all subjects.

B. Data recording

Data recordings were performed after the patient had rested for 5 minutes in a semi-recumbent position on the dialysis chair. Continuous ECG and PPG were recorded for 6 minutes followed by a blood pressure measurement before the start of dialysis and at the end of dialysis. The ECG was recorded in lead II configuration using a bio-amplifier (ST4400, ADInstruments, Sydney, Australia) and blood pressure measurement was performed using a digital sphygmomanometer embedded in the dialysis machine. The PPG waveform was recorded from the tip of the index finger of the non-fistula access hand, using a reflection mode infra-red finger probe, utilizing light at 940 nm (MLT1020FC, ADInstruments, Sydney, Australia). The recorded signals were digitized at a sampling rate of 1 kHz using the Powerlab data acquisition system (ST4400, ADInstruments, Sydney, Australia); no high pass filtering was performed before sampling in order to preserve the DC component in the PPG waveform.

C. Signal processing and feature extraction

All signal processing and feature extraction was implemented in Matlab (Natick, MA, USA). For ECG and PPG data analysis, a 4 minute artifact-free and stationary segment was selected from each recording. The PPG signal was first low-pass filtered using a Butterworth low pass filter with a 3 dB at 18 Hz. Zero phase filtering was implemented by filtering the signal in both forward and reverse directions to eliminate phase distortion. Following this, systolic peaks and diastolic troughs (baseline) were identified from the PPG signal, as illustrated in figure 1. The amplitude corresponds to the difference between the peak and trough values after baseline removal by subtraction of a 2 s moving average [10]. R-wave peaks were detected from the ECG signal using a set of programming routines involving low-pass filtering, differentiation, and threshold-based peak detection, R-R interval (RRi) and HR were computed accordingly.

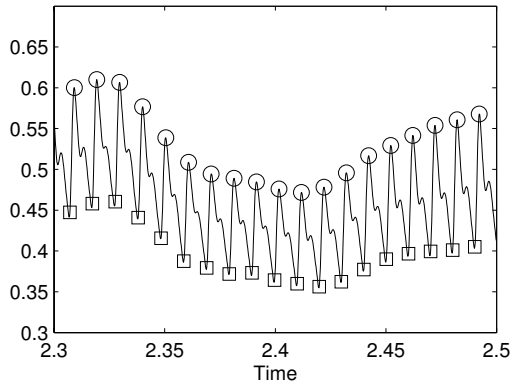

Fig. 1. Detected systolic peaks represented by circles and diastolic troughs represented by squares, from a finger photoplethysmographic (PPG) waveform segment.

D. Frequency spectrum analysis

The beat-to-beat sequence of RRi and finger PPG waveform features were first interpolated to evenly spaced samples in time, then downsampled to 2 Hz after appropriate low-pass filtering. The very low frequency trend was removed from the downsampled signal [10]. The power spectra of HRV and finger PPGV were computed by a 2048-pt Fast Fourier Transform (FFT) of the windowed autocorrelation of RRi and PPGV features, based on the Blackman Tukey method.

The power spectra of HRV and PPGV were divided into an LF band (0.04 - 0.145 Hz) and an HF band (0.145 - 0.45 Hz) [5], [8], [9], [10]. In HRV, the LF band is thought to be influenced by the baroreceptor reflex and reflects the combined effect of sympathetic and vagal modulation; whilst the HF band is thought to reflect respiratory frequency vagal modulation [13], [14]. The LF/HF ratio of HRV, which is considered as an index of sympathovagal balance by some investigators, was also computed [5]. In PPGV, the LF band is considered to reflect mainly sympathetic nervous system influence on peripheral vessels, with the HF band representing mechanical effects of respiration [8]. A more specific identification of sympathetic vascular modulation by autonomic mechanisms may be measured using the MF band (0.08 - 0.145 Hz) [4], [9], [10]. The power in each band

TABLE II
CHANGES IN THE VITAL SIGN MEASUREMENTS

Value	Pre-dialysis	End of dialysis	p value
HR	69 ± 3	70.6 ± 2.9	0.6
SBP	149 ± 8.3	155 ± 12.5	0.5
DBP	70.1 ± 4.1	71.2 ± 4.4	0.9

TABLE III
CHANGES IN THE HRV SPECTRAL MEASURES

	Pre-dialysis	End of dialysis	p value
RR	862 ± 44.1	866.8 ± 30.6	0.9
LF (nu)	47.7 ± 7	53.1 ± 7.5	0.5
HF (nu)	52.2 ± 7.5	46.9 ± 7.5	0.5
LF au	138.1 ± 59.2	131.9 ± 45.4	0.9
HF au	87.8 ± 30.7	89.2 ± 37.4	0.9
LF/HF	1.6 ± 0.57	2 ± 0.63	0.2

was calculated by integration of the power spectrum over the specified frequency range, and the powers were expressed in normalized units (nu), after division by the sum of powers in LF and HF and multiplied by 100, and were denoted as LFnu, MFnu and HFnu. The band powers of PPGV were also expressed in mean-scaled units (msu) after division by the square of the mean pulse amplitude, multiplication by 100, and were then denoted as LFmsu, MFmsu and HFmsu.

III. RESULTS AND DISCUSSION

The results are based on data sets from 11 patients, the data recording from one of the patient was rejected due to severe artifacts. All results are expressed as mean ± standard error (SE). Table II reports the change in the heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) at pre-dialysis and end of dialysis. Based on the statistical results, no significant change was observed in any of these vital sign measurements indicating that all hemodialysis sessions were stable with no hypotension phase.

Table III tabulates the changes in the RRi and its spectral measures at pre-dialysis and end of dialysis. Although there was no significant change in any of the spectral powers, the results show an increase in the LFnu which indicates a dominance of sympathetic over parasympathetic nerve activity. Our results are consistent with previous studies into spectral analysis of HRV that reported reflex excitation of sympathetic efferent activity, represented by augmentation of the normalized LF power of HRV, and inhibition of parasympathetic activity represented by the HF power of HRV [6], [7], [15], [16], [17] in stable patients, due to loss of blood volume during hemodialysis.

Fig. 2 and 3 shows the actual power spectrum for PPG baseline and amplitude variability for one of the patient. Table IV shows the changes in the spectral measures of PPGV. All frequency bands showed a significant increase at the end of dialysis compared to pre-dialysis for amplitude variability when expressed in mean-scaled units. For baseline variability LF and MF spectral powers also showed

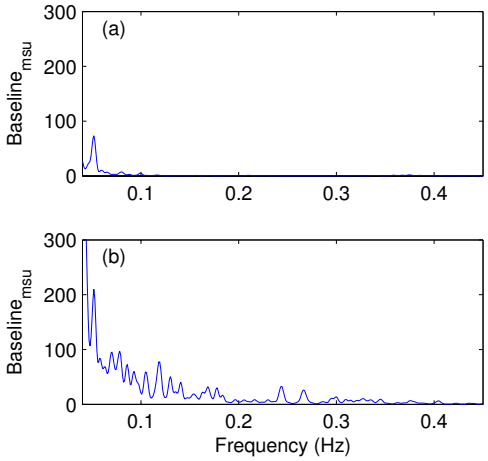

Fig. 2. Frequency spectrum of baseline PPGV at (a) pre-dialysis and (b) end of dialysis for one patient.

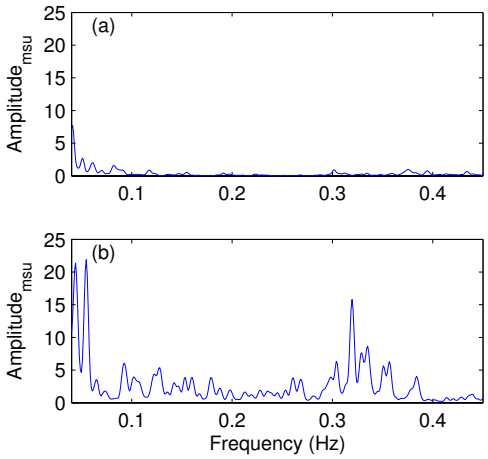

Fig. 3. Frequency spectrum of amplitude PPGV at (a) pre-dialysis and (b) end of dialysis for one patient.

a significant increase when expressed in mean-scaled units. The increases in LF and MF powers of PPGV suggest an enhancement of sympathetic control over peripheral vasculature, which may be associated with the compensatory response to volume unloading [10]. Similar increase in LF power has been observed in blood pressure variability in stable patients during the late stage of hemodialysis [7]. The augmentation of HF power in PPGV may suggest a preload reduction due to volume removal. This change has been noted in mechanically ventilated patients and in healthy blood donors subsequent to volume removal [10], [13], [14].

It should be noted that the changes in the spectral measures of PPGV were only evident when expressed in mean-scaled units and not in normalized units. One reason would be that a decrease in finger pulse volume may have some role in amplification of the PPGV spectral measures, as the derivation of the means scaled units relied on the band powers of PPGV

TABLE IV

CHANGES IN THE PPGV SPECTRAL MEASURES

		Pre-dialysis	End of dialysis	p value
Baseline	LF msu	2.5 ± 0.5	19.2 ± 5.5	0.01*
	MF msu	0.6 ± 0.10	5.9 ± 2.0	0.02*
	HF msu	0.5 ± 0.16	4.1 ± 1.6	0.05
	LF nu	83.4 ± 3.2	84.6 ± 2.1	0.74
	MF nu	19.7 ± 2.1	24.7 ± 3.0	0.24
Amplitude	LF msu	0.30 ± 0.13	0.60 ± 0.17	0.006**
	MF msu	0.10 ± 0.03	0.20 ± 0.05	0.03*
	HF msu	0.10 ± 0.03	0.5 ± 0.1	0.02 *
	LF nu	61.2 ± 6.1	52.5 ± 5.0	0.2
	MF nu	21.1 ± 1.3	18.8 ± 1.5	0.25

* $p < 0.05$
** $p < 0.01$

being divided by the square of the mean pulse volume. This decrease in finger pulse volume may be explained by stroke volume reduction and by vasoconstriction in the finger, which are typical physiological responses to volume loss [10], [18]. Another reason would be the concomitant increase of LF and HF powers during volume removal, such that the ratio of the LF to HF powers remained unchanged or even decreased. The insensitivity of PPGV normalized spectral powers to blood loss as compared to the spectral powers expressed in mean-scaled units was also noticed in Middleton et al. [10]. The implication would be that unlike HRV, the normalization procedure might not be the best way to represent the changes in PPGV during blood volume removal, either in a dialysis setting or in a blood donation setting.

Some of the limitations of the current work are worth mentioning here. This study was constrained to hemodynamically stable patients. Future studies should also consider patients with a history of dialysis complicated by hypotensive episodes. The current study was based on comparison between the pre-dialysis and end of dialysis with no information regarding the changes in the spectral measures during hemodialysis. Further studies should consider frequent measurements within the dialysis session to further investigate if these changes occur progressively with fluid loss or not.

IV. CONCLUSIONS

The results of this study demonstrate that spectral analysis of finger PPGV may provide a novel method to assess peripheral circulatory response to volume withdrawal following hemodialysis. The augmentation of LF and MF powers may indicate an activation of sympathetic control over peripheral vasculature, while the increase in respiratory-related HF power is likely to signify preload reduction. However, since the current study was based on comparison between pre-dialysis and end of dialysis, further studies are required to assess these changes at different stages during hemodialysis. Also this study was based on hemodynamically stable patients and the utility of PPGV for monitoring unstable patients who are at risk of intradialytic complications is yet to be explored.

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