Hemodynamic Effects of Chronic Hemodialysis Therapy Assessed by Pulse Waveform Analysis

Crystal A. Gadegbeku, M. Zakarea Shrayyef, and Michael E. Ullian

Cardiovascular responses to hemodialysis have been characterized by invasive monitoring techniques. These techniques are not feasible for evaluation of hemodynamic status during dialysis in the outpatient setting. In this study, we used pulse waveform analysis (PWA), a noninvasive tool designed for the ambulatory setting, to assess hemodynamic responses of dialysis treatments in 27 stable subjects with end-stage renal disease receiving chronic hemodialysis. In our population, systolic, diastolic, and pulse pressures were unaffected by dialysis despite the mean fluid removal of 3.0 ± 0.2 kg. However, using PWA, we observed that stroke volume and cardiac output progressively declined by 17% to 19% (P < .001) with a concomitant increase in systemic vascular resistance by 22% from 1654 ± 88 to 2020 ± 121 dynes · sec · cm⁻⁵ (P < .001). Also, we observed a significant reduction in small artery compliance from 4.7 ± 0.5 to 3.3 ± 0.4 mL · mm Hg⁻¹ · 100 (P = .01), whereas large artery elasticity was unaffected. These findings suggest that changes in small artery vascular compliance contribute to the elevation in systemic vascular resistance during dialysis. This study confirms that hemodynamic adaptations to the dialysis procedure can be detected using PWA and are consistent with data obtained by invasive monitoring techniques. Furthermore, the observed reduction in vascular compliance in response to dialysis may contribute to the high cardiovascular risk in patients undergoing chronic hemodialysis therapy. Am J Hypertens 2003;16:814 – 817 © 2003 American Journal of Hypertension, Ltd.

Key Words: Blood pressure, hemodialysis, vascular compliance, cardiac output.

Chronic hemodialysis is a life-sustaining therapy for more than 200,000 Americans with end-stage renal disease.¹ The fluid and electrolyte shifts provoked during the hemodialysis procedure are known to cause acute hemodynamic effects, which have been characterized by various cardiovascular monitoring techniques. These techniques are complex, invasive, and limited to the research setting. Pulse waveform analysis (PWA) is a simple noninvasive technique designed for outpatient use that can be used to assess multiple hemodynamic variables. This technique, which has been validated in hypertensives and normotensive subjects, estimates hemodynamic parameters by analyzing the pressure-generated pulse contour based on a mathematical model of the arterial circulation.² In addition to measuring cardiac output and systemic vascular resistance, this technique can be used to assess large and small artery compliance. Arterial compliance has been found to be abnormally reduced in hemodialysis patients,³–⁶ but less is known about the acute effects of dialysis on proximal and distal vascular properties. Left ventricular hypertrophy, a significant risk factor for death in dialysis patients,⁷ is associated with arterial stiffness.⁵,⁸ Therefore, greater insight into changes in vascular compliance during dialysis may be important in understanding the vascular adaptations that predispose these patients to cardiovascular disease. Given the growing body of literature to support the feasibility of this technique in an outpatient setting, we characterized the hemodynamic effects of hemodialysis therapy using PWA in a stable outpatient dialysis population.

Methods

Study Population

Chronic end-stage renal disease patients attending an outpatient hemodialysis unit of Dialysis Clinics, Incorporated, in Charleston, South Carolina, were invited to participate in this study. Patients on chronic hemodialysis for at least 6 months were included in the study. Patients were excluded if there were clinical signs or symptoms of untreated or unresolved infection or illness, blood pressure (BP) more than 200/110 mm Hg, systolic BP less than 90 mm Hg, or if antihypertensive medications had been used.
changed within 3 weeks. Also, subjects who did not have a palpable radial artery pulse for PWA secondary to multiple forearm angioaccesses were excluded from the study. Subjects provided written informed consent, approved by the Institutional Review Board and were compensated for participation.

**Physiologic Measurements**

The HDI/PulseWave CR-2000 Research CardioVascular Profiling System (Hypertension Diagnostics, Inc., Eagan, MN) was used to determine BP, heart rate, stroke volume, cardiac output, systemic vascular resistance, capacitive compliance, C1 (an estimate of large artery elasticity), and reflective compliance, C2 (an estimate of small artery elasticity). This technique, which analyzes the signal-averaged radial artery waveform based on a modified Windkessel model, correlates well with other methods used to measure hemodynamic parameters in humans.9

The arterial PulseWave Sensor was stabilized over the nonangioaccess radial artery after the BP cuff was placed on the upper arm. Hemodynamic measurements were obtained after patient rested for 5 min in a seated position in the dialysis chair (baseline). These measurements were compared to hemodynamic data obtained at time 0 (blood initially entering extracorporeal circuit), 30, 60, 90, 120, 150, 180 min, and recovery (5 min after blood was returned from the extracorporeal circuit). Seventeen of the 27 patients (63%) were dialyzed long enough to obtain values at 180 min. Hemodynamic measurements at all other time points including recovery were obtained from all 27 patients.

**Data Analysis**

Data are presented as mean ± SEM. Results at each time point were compared to baseline data using a two-sided paired t test with Bonferroni multiple comparisons procedure.

**Results**

**Patient Characteristics**

Twenty-seven patients on chronic hemodialysis were studied, as shown in Table 1. Reflecting the regional demographics of end-stage renal disease, the majority of patients were African American, and hypertension and diabetes were the most common causes of end-stage renal disease. The greater number of women compared to men in this study reflects the patient population at this local dialysis unit (63% women in entire dialysis unit). Thirty-three subjects were screened and 27 subjects completed the study. Three patients were excluded for lack of palpable radial pulses, and 3 for failing to meet BP criteria.

**Hemodynamic Responses to Hemodialysis**

On average, systolic, diastolic, mean, and pulse pressures did not change throughout dialysis despite the average fluid removal of 3.0 ± 0.2 kg (Fig. 1A). For the most part, heart rate was unaffected by dialysis except for an initial, transient decrease from 73 ± 2 to 71 ± 2 beats/min (P = .01) (Fig. 1B). On the other hand, stroke volume and correspondingly, cardiac output progressively declined to values, at the end of dialysis, that were 17% and 19% lower than those at baseline (both P ≤ .001) (Fig. 1C,D). Both parameters tended to rebound after return of blood volume from the extracorporeal circuit but remained significantly lower than baseline values. Concomitantly, systemic vascular resistance progressively increased by 22% from a mean baseline value of 1654 ± 88 to 2020 ± 121 dynes · sec · cm⁻² at the end of dialysis (P ≤ .001) (Fig. 1E). In recovery, systemic vascular resistance also rebounded toward baseline values, as observed with stroke volume and cardiac output. However, unlike stroke volume and cardiac output, the mean systemic resistance at recovery was not statistically different from baseline (P = .34).

Large artery compliance, C1, remained constant during hemodialysis (Fig. 1F). In contrast, small artery compliance, C2, was significantly reduced from a mean predialysis measurement of 4.7 ± 0.5 to 3.3 ± 0.4 mL · mm Hg⁻¹ · 100 at 150 min (P = .009) and sustained in recovery (3.5 ± 0.5 mL · mm Hg⁻¹ · 100, P = .01) (Fig. 1F).

**Discussion**

The major observation in this study is that cardiovascular responses can be measured during outpatient hemodialysis with the use of PWA. With this novel technique, we observed that BP was maintained during dialysis despite significant decreases in stroke volume and cardiac output due to compensatory increases in systemic vascular resistance. Furthermore, our findings suggest that reductions in small artery compliance play a significant role in the elevation of systemic vascular resistance.

The PWA has been used in a variety of hypertensive and normotensive patient populations to determine hemodynamic parameters beyond the measurement of BP. This technique is reproducible and closely correlates with estimates of cardiac output and vascular compliance obtained from the dye-dilution technique.9

### Table 1. Patient characteristics

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<tr>
<td>N</td>
<td>27</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>9/18</td>
</tr>
<tr>
<td>Age (y)</td>
<td>55 ± 3 (26–85)</td>
</tr>
<tr>
<td>Race (white/African American)</td>
<td>2/23</td>
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<tr>
<td>Length of time on HD (mo)</td>
<td>47 ± 7 (2–117)</td>
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<tr>
<td>Etiology of renal disease</td>
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</tr>
<tr>
<td>Diabetes</td>
<td>8 (37%)</td>
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<tr>
<td>Hypertension</td>
<td>11 (41%)</td>
</tr>
<tr>
<td>Other</td>
<td>6 (22%)</td>
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<tr>
<td>Fluid removed (kg)</td>
<td>3.0 ± 0.2 (0.8–5.3)</td>
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Range in parentheses.
Our study is the largest of three studies using some form of PWA to measure hemodynamic responses during dialysis. Bos et al.\textsuperscript{10} used a finger-pressure PWA system and found similar changes in stroke volume, cardiac output, and systemic vascular resistance in 9 patients. However, in contrast to our findings, they observed significant decreases in BP and pulse pressure. In obtaining these data, they admitted that finger pressures were difficult to measure during hemodialysis in some patients, which may have led to population bias. In addition, measurements derived from finger circulation may not adequately predict central cardiovascular changes. In our study, we were successful in obtaining waveform data from all subjects using the HDI system. This system uses more proximal sites for measurements of BP (the upper arm cuff) and PWA (the radial artery), which may lead to more accurate assessments of central hemodynamic responses associated with dialysis.

In support of our findings, Cohen and Townsend\textsuperscript{11} found no change in BP, pulse pressure, heart rate, or C1, and similar reductions in C2 using the same PWA system. In our group, C1 estimates (Fig. 1F) are similar to values obtained in other hypertensive populations.\textsuperscript{12,13} However, the acute removal of blood volume did not result in further significant reductions in large vessel tone, which may reflect the extensive large artery stiffness secondary to vascular remodeling, previously described in hemodialysis patients.\textsuperscript{4–6}

On the other hand, the dialysis procedure is associated with reductions in C2, which may be a compensatory vascular response to preserve BP (Fig. 1F). The reduced C2 values are similar to estimates observed in uncontrolled hypertensive subjects (12). Growing data support that reduced small artery compliance is associated with vascular disease in the general population\textsuperscript{3} and left ventricular hypertrophy, a cardiovascular risk factor, in dialysis patients.\textsuperscript{8} In the long term, the acute reductions in already low small vessel compliances at each dialysis may contribute to the high cardiovascular risk in dialysis patients. Despite significant reductions in small artery compliance in the study by Cohen and Townsend,\textsuperscript{11} they did not observe a statistically significant increase in systemic vascular resistance. Our study was adequately powered to demonstrate that systemic resistance is significantly increased, which can be explained by vasoconstriction of resistance vessels, represented by C2. Further comparison between our study and the study by Cohen and Townsend cannot be made because they did not report other hemodynamic variables. In general, our study extends the data demonstrating that the hemodynamic effects of dialysis can be characterized by this noninvasive novel technique.

As observed in our study, the progressive reduction in stroke volume and cardiac output has been described in recent studies, which used invasive cardiovascular monitoring. Several investigators\textsuperscript{14–17} have noted direct correlations between changes in total blood volume and stroke volume/cardiac output. Furthermore, an approximate 20% decline in stroke volume and cardiac output with a compensatory increase in systemic vascular resistance has been demonstrated using thermodilution in hemodynamically
cally stable patients in several studies.15–17 Therefore, our data are consistent with published results obtained invasively and suggest that PWA is accurate in the assessment of cardiovascular responses during hemodialysis.

There are several limitations in this study. First, concurrent invasive measures along with PWA will be necessary to confirm the accuracy of PWA during dialysis. Also, we did not perform serial measurements of total blood volume to assess the relationship between changes in cardiac function and blood volume, which has been done with other cardiovascular monitoring techniques. In addition, vasoactive electrolytes, like potassium and calcium, were not assessed in this study, which have been shown to influence vascular compliance in dialysis patients.4

Nonetheless, PWA was found to be a feasible noninvasive technique when applied during dialysis for the assessment of cardiovascular function. Moreover, results are similar to hemodynamic responses determined invasively. Potentially, this technique could be useful in assessment of hemodynamic instability and for individual adjustment of the dialysis prescription to optimize BP status. More important, because patients with end-stage renal disease have multiple cardiac risk factors and develop accelerated atherosclerosis, longitudinal studies focusing on arterial compliance should be pursued to determine whether the PWA technique can be a useful tool in identifying patients at risk for cardiovascular events.

**Acknowledgments**

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**References**


