

# Comparison of arterial stiffness in end-stage renal disease patients treated with peritoneal dialysis or hemodialysis

Paweł Stróżecki, Rafał Donderski, Anna Kardymowicz, Jacek Manitius

Department of Nephrology, Hypertension, and Internal Diseases, Nicolaus Copernicus University, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Bydgoszcz, Poland

## KEY WORDS

arterial stiffness,  
hemodialysis,  
peritoneal dialysis,  
pulse wave velocity

## ABSTRACT

**INTRODUCTION** Dialysis patients have increased arterial stiffness. The results of the available studies comparing arterial stiffness between patients on peritoneal dialysis (PD) and those on hemodialysis (HD) are inconsistent.

**OBJECTIVES** The aim of the study was to compare pulse wave velocity (PWV) in PD and HD patients and to compare the value of measured PWV ( $PWV_M$ ) with the theoretical value of this parameter ( $PWV_T$ ).

**PATIENTS AND METHODS** The study group involved 35 PD and 26 HD patients in whom the carotid-femoral  $PWV_M$  was measured using the Complior device. In all patients  $PWV_T$  was calculated using the equation developed by Blacher et al.

**RESULTS** Patients did not differ significantly in age, sex, and the prevalence of diabetes. There were no significant differences in  $PWV_M$  (PD:  $12.1 \pm 3.3$  vs. HD:  $12.0 \pm 3.0$  m/s) and  $PWV_T$  (PD:  $10.0 \pm 1.4$  vs. HD:  $9.9 \pm 1.2$  m/s) between PD and HD patients.  $PWV_M$  was significantly higher than  $PWV_T$  both in PD and HD patients. Diastolic blood pressure and mean arterial pressure were higher in PD patients, but systolic blood pressure and pulse pressure did not differ significantly between the groups. PD patients received more antihypertensive drugs than HD patients ( $3 \pm 1$  vs.  $2 \pm 1$ ;  $P < 0.05$ ).

**CONCLUSIONS** Arterial stiffness is equally increased in PD and HD patients.  $PWV_M$  is higher than  $PWV_T$  in PD and HD patients, which may reflect accelerated arterial aging in patients on dialysis.

**INTRODUCTION** Patients on dialysis are characterized by high cardiovascular (CV) morbidity and mortality.<sup>1</sup> Mortality rate of dialyzed patients in Poland in the year 2007 was 14.3%, and CV diseases accounted for over 50% of deaths.<sup>2</sup> Arterial stiffness is increased in patients on dialysis, both hemodialysis (HD) and peritoneal dialysis (PD), compared with healthy controls.<sup>3,4</sup> Pulse wave velocity (PWV) measured between the carotid and femoral artery is the gold standard for the assessment of arterial stiffness.<sup>5</sup> PWV was shown to be an independent risk factor for death in patients on HD.<sup>6</sup> The results of studies comparing PWV between PD and HD patients are inconsistent. PWV was the same,<sup>7-9</sup> lower,<sup>10,11</sup> or higher<sup>12</sup> in PD patients compared with HD patients.

Based on the analysis of PWV results, Blacher et al.<sup>13</sup> developed an equation to calculate

the theoretical value of PWV ( $PWV_T$ ) using several clinical parameters, including age, sex, mean arterial pressure (MAP), and heart period:  $PWV_T = 0.0793 \times \text{age} + 0.0427 \times \text{MAP} - 0.0014 \times \text{heart period (ms)} - 0.415 \times \text{sex (F = 2, M = 1)} + 2.934$ . The equation was derived from a multivariate analysis in a population of 469 patients without end-stage renal disease (ESRD). It was subsequently applied to patients with ESRD to obtain  $PWV_T$ . Then  $PWV_T$  was compared with the measured PWV ( $PWV_M$ ), and the PWV index was calculated ( $PWV \text{ index} = PWV_M - PWV_T$ ). The study revealed that the PWV index was a strong predictor of CV and overall mortality in the population of ESRD patients undergoing HD: the higher the  $PWV_M$  when compared with the  $PWV_T$ , the worse the prognosis.<sup>13</sup> It also follows from the equation that PWV increases with age by 0.8 m/s for each decade of life.

## Correspondence to:

Paweł Stróżecki, MD, PhD,  
Klinika Nefrologii, Nadciśnienia  
Tętniczego i Chorób Wewnętrznych,  
ul. M. Skłodowskiej-Curie 9,  
85-094 Bydgoszcz, Poland,  
phone: +48-52-585-45-51,  
fax: +48-52-585-40-30,

e-mail: st\_pawel@cm.umk.pl

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**TABLE 1** Clinical characteristics of patients on peritoneal dialysis and hemodialysis

	PD (n = 35)	HD (n = 26)	P
age, y	57 ± 13	60 ± 14	NS
men, n (%)	18 (51)	16 (61)	NS
hypertension, n (%)	30 (86)	22 (85)	NS
diabetes, n (%)	9 (26)	7 (27)	NS
duration of dialysis therapy, mo	17 ± 23	61 ± 55	<0.001
BMI, kg/m <sup>2</sup>	24.5 ± 4.2	25.7 ± 5.0	NS
waist circumference, cm	89 ± 13	92 ± 12	NS
SBP, mmHg	139 ± 20	134 ± 28	NS
DBP, mmHg	82 ± 14	71 ± 10	<0.01
MAP, mmHg	101 ± 15	93 ± 14	<0.05
PP, mmHg	57 ± 15	62 ± 25	NS
heart rate, 1/min	73 ± 12	74 ± 12	NS
antihypertensive drugs, n	3 ± 1	2 ± 1	<0.05
hemoglobin, g/dl	11.2 ± 1.2	11.3 ± 1.1	NS
calcium, mmol/l	2.26 ± 0.16	2.24 ± 0.22	NS
phosphorus, mmol/l	1.81 ± 0.48	1.68 ± 0.50	NS
PTH, pg/ml	377 ± 328	391 ± 324	NS
albumin, g/dl	3.73 ± 0.46	3.93 ± 0.51	NS
PWV <sub>M</sub> , m/s	12.1 ± 3.3	12.0 ± 3.0	NS
PWV <sub>T</sub> , m/s	10.0 ± 1.4	9.9 ± 1.2	NS

Abbreviations: BMI – body mass index, DBP – diastolic blood pressure, HD – hemodialysis, MAP – mean arterial pressure, NS – nonsignificant, PD – peritoneal dialysis, PP – pulse pressure, PTH – parathormone, PWV<sub>M</sub> – measured pulse wave velocity, PWV<sub>T</sub> – theoretical pulse wave velocity, SBP – systolic blood pressure

The aim of the present study was to compare PWV<sub>M</sub> between PD and HD patients and to compare PWV<sub>M</sub> with PWV<sub>T</sub> calculated using the above equation.

**PATIENTS AND METHODS** The study population included 61 patients on dialysis: 35 on PD and 26 on HD. Carotid-femoral PWV was measured in all subjects. First, it was measured in PD patients dialyzed in a single centre. All PD patients agreed to participate in the study. The measurement was performed on the day of routine appointment in an outpatient clinic, between 8 a.m. and noon. Then, 26 HD patients matched for age, sex, and the prevalence of diabetes were recruited from a group of 120 HD patients. The inclusion criteria for HD patients were informed consent and PWV measurement taken between 8.00 a.m. and noon on the day of a midweek HD session.

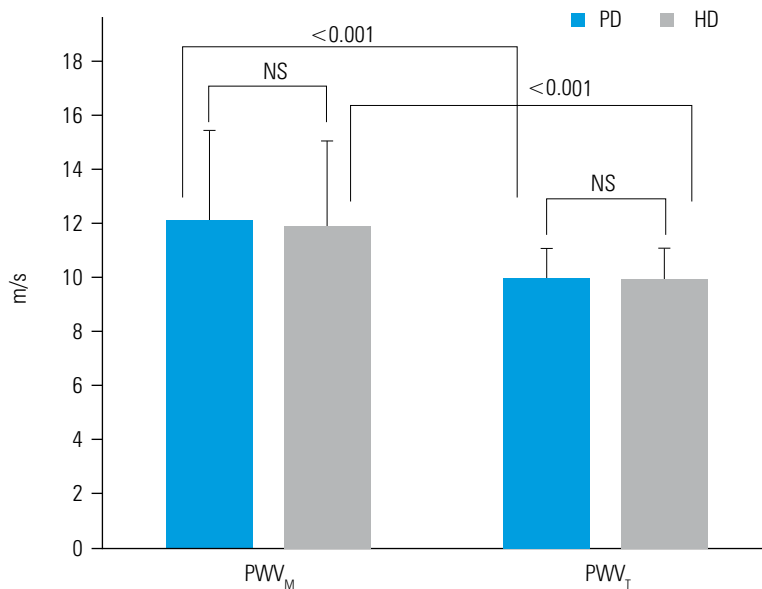
The study was approved by the local Ethics Committee. Informed consent was obtained from each participant.

Patients on HD were dialyzed 3 times a week and a single session took from 4 to 5 hours. Duration of HD session, type of dialyzer, and blood flow were adjusted to obtain Kt/V >1.2. The mean (± standard deviation [SD]) Kt/V calculated using the Daugirdas formula was 1.36 ± 0.17. Of all PD patients, 29 were dialyzed with automated PD (nocturnal peritoneal dialysis or continuous cyclic peritoneal dialysis [CCPD]) and 6 with continuous

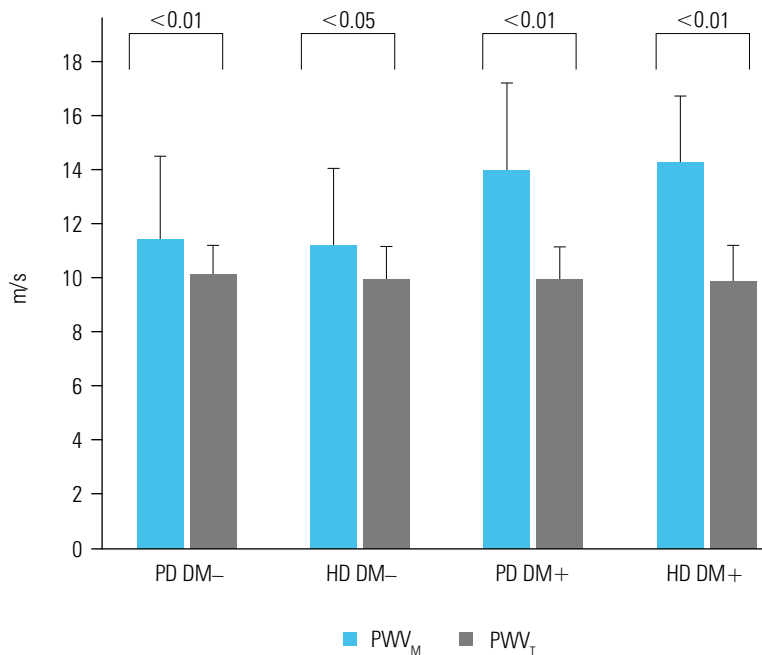
ambulatory peritoneal dialysis (CAPD). Weekly Kt/V in the PD group was 2.53 ± 0.57.

All subjects underwent clinical assessment and the use of antihypertensive therapy was analyzed. Blood pressure (BP) was measured using mercury sphygmomanometer immediately before PWV measurement. Based on systolic (SBP) and diastolic (DBP) BP, pulse pressure (PP) and MAP were calculated (PP = SBP – DBP and MAP = DBP + 1/3 PP, respectively). Heart rate and anthropometric measurements (waist circumference, height, body mass) were obtained. Laboratory variables including hemoglobin, serum calcium, phosphorus, parathormone, and albumin levels were measured. Clinical characteristics of the study group are presented in **TABLE 1**.

**Pulse wave velocity** Carotid-femoral PWV was measured using the Complior® device (Artech Medical, Pantin, France). Two transducers – one positioned over the carotid artery and the other over the femoral artery – were used to measure time delay between pulse waves. Time delay was measured at 10 successive beats and averaged. The distance between the carotid (suprasternal notch) and femoral arteries was measured externally. PWV was calculated according to the formula: PWV = distance (m)/time delay (s). PWV measurements were taken in duplicate and averaged. In CAPD and CCPD patients, PWV was measured with full abdomen, but according to Covic et al.,<sup>12</sup> this does not affect the results.



**FIGURE 1** Measured and theoretical pulse wave velocity in patients on peritoneal dialysis and hemodialysis  
Abbreviations: see TABLE 1



**FIGURE 2** Comparison of measured and theoretical pulse wave velocity in nondiabetic (DM-) and diabetic (DM+) patients on peritoneal dialysis and hemodialysis  
Abbreviations: see TABLE 1

In HD patients, PWV was measured before a mid-week HD session.

**Statistical analysis** Data are presented as mean  $\pm$  SD. Distribution of variables was analyzed using the Shapiro-Wilk test. Statistical analysis was performed using the Student's *t*-test. If the variable was not normally distributed, the Mann-Whitney *U* test was used. Qualitative data were compared using the  $\chi^2$  test. A linear correlation between variables was analyzed.  $P < 0.05$  was considered statistically significant.

**TABLE 2** Comparison of measured pulse wave velocity in dialysis patients with and without diabetes

PWV <sub>M</sub> m/s	DM-	DM+	<i>P</i>
in PD patients	11.4 $\pm$ 3.1	14.0 $\pm$ 3.2	<0.05
in HD patients	11.2 $\pm$ 2.8	14.2 $\pm$ 2.5	<0.05

Abbreviations: see TABLE 1 and FIGURE 2

**RESULTS** There were no significant differences in PWV<sub>M</sub> or PWV<sub>T</sub> between PD and HD patients (FIGURE 1). Duration of dialysis therapy was significantly longer in HD patients. DBP and MAP were significantly higher in PD patients, despite the fact that they received more antihypertensive drugs compared with HD patients. PWV<sub>M</sub> was significantly higher than PWV<sub>T</sub> both in PD and HD patients ( $P < 0.001$ ). PWV<sub>M</sub> was significantly higher in diabetic PD and diabetic HD patients compared with nondiabetic patients (TABLE 2). PWV<sub>M</sub> was also significantly higher than PWV<sub>T</sub> in the subgroups of nondiabetic and diabetic patients, both on PD and HD (FIGURE 2). A significant positive correlation was observed between PWV<sub>M</sub> and age and PP in both groups (TABLE 3). A positive correlation between PWV<sub>M</sub> and SBP, and an inverse correlation between PWV<sub>M</sub> and DBP did not reach statistical significance. There was no correlation between the duration of renal replacement therapy and PWV<sub>M</sub> ( $r = -0.07$  for PD patients;  $r = 0.07$  for HD patients).

**DISCUSSION** The effect of PD on CV system is considerably different from that of HD. The preferred dialysis modality in patients with chronic kidney disease (CKD) and CV diseases is still a matter of debate. Another question is which dialysis modality is associated with lower risk of new CV events in patients with ESRD.<sup>14,15</sup>

PD may provide better fluid and BP control compared with HD, particularly during the first years of therapy, due to continuous ultrafiltration, hemodynamic stability, and lack of arteriovenous fistula.<sup>14</sup> Moreover, residual renal function and diuresis are maintained longer in PD patients. However, after several years of PD, when peritoneal ultrafiltration capacity and residual diuresis are reduced, worsening of BP control and hypervolemia may occur.<sup>14</sup> Other CV risk factors are also present in PD patients, including atherogenic lipid profile, accumulation of uremic toxins such as advanced glycation end-products, and chronic inflammation associated with peritoneal fluid bioincompatibility related to glucose degradation products.<sup>12,16,17</sup> Several epidemiological studies revealed higher mortality rate in PD patients than in HD patients.<sup>1,18</sup>

PWV – a measure of arterial stiffness – is an independent predictor of death and CV morbidity in patients on HD.<sup>6</sup> In a recent study, it has been shown that arterial stiffness, assessed as aortic stiffness index  $\beta$ , is an independent predictor of CV events and death in patients on PD.<sup>19</sup>

**TABLE 3** Correlation coefficients between the measured pulse wave velocity and clinical and laboratory parameters

Parameter	P <sub>WM</sub> PD		P <sub>WM</sub> HD	
	r	P	r	P
age, y	0.63	<0.001	0.51	<0.01
waist, cm	0.27	0.11	-0.24	0.24
SBP, mmHg	0.30	0.08	0.35	0.08
DBP, mmHg	-0.22	0.23	-0.37	0.07
MAP, mmHg	0.00	0.99	0.06	0.77
PP, mmHg	0.63	<0.001	0.55	<0.01
BMI, kg/m <sup>2</sup>	0.28	0.11	-0.14	0.49
heart rate, 1/min	0.01	0.95	-0.22	0.27
hemoglobin, g/dl	-0.15	0.43	0.19	0.35
calcium, mmol/l	-0.22	0.23	-0.07	0.75
phosphorus, mmol/l	-0.22	0.23	-0.07	0.75
PTH, pg/dl	-0.23	0.21	0.14	0.48
albumin, g/dl	-0.18	0.34	-0.28	0.16

Abbreviations: see [TABLE 1](#)

A number of studies compared arterial stiffness between PD and HD patients.<sup>7-12</sup> However, the results are inconsistent and do not allow to conclude which dialysis modality is associated with higher arterial stiffness. In those studies, PWV in PD patients was the same,<sup>7-9</sup> lower,<sup>10,11</sup> or higher<sup>12</sup> when compared with HD patients. In 3 of those studies, the carotid-femoral PWV (cfPWV) was measured, while in other studies the brachial-ankle PWV (baPWV) or carotid-radial PWV were used. The measurement of PWV between the carotid and femoral arteries is considered to be the gold standard for the assessment of arterial stiffness.<sup>5</sup> It was clearly shown that this parameter is an independent predictor of all-cause and CV mortality in the general population, patients with hypertension, diabetes, and ESRD.<sup>5,6</sup>

In our study, we applied the reference method of arterial stiffness measurement and the current results suggest that there is no difference in arterial stiffness between PD and HD patients. Similar results were obtained by Hermans et al.<sup>20</sup> They showed that cfPWV did not differ significantly between PD and HD patients (9.4 ± 2.6 vs. 10.1 ± 3.0; nonsignificant). However, despite similar clinical characteristics of the study population, cfPWV was higher in our study (12.1 ± 3.3 in PD patients; 12.0 ± 3.0 in HD patients). This discrepancy may result from the use of different diagnostic devices (Sphygmo-Cor vs. Complior, respectively). A study comparing different devices used to measure cfPWV revealed that the results obtained with Complior are higher than those obtained using Sphygmo-Cor, with a difference as high as 2.0 m/s.<sup>20</sup>

Another study that compared arterial stiffness measured in vivo as PWV and in vitro as stiffness of the inferior epigastric artery harvested during kidney transplantation showed no significant differences between PD and HD patients.<sup>7</sup> However, a trend for higher arterial stiffness in PD patients was observed.<sup>7</sup> PWV measured in the upper limb

(between the carotid and radial arteries) and in the lower limb (between the femoral and dorsalis pedis arteries) also did not differ significantly between PD patients, HD patients, and nondialyzed patients with CKD stage 4.<sup>9</sup> Nevertheless, it should be noted that the structure of the arterial wall differs between the aorta and the arteries of the extremities, and the course of arterial remodelling differs between elastic and muscular arteries.

On the other hand, in a study by Covic et al.,<sup>12</sup> higher arterial stiffness was demonstrated in PD patients compared with HD patients. Increased arterial stiffness was attributed to increased vascular endothelial dysfunction in PD patients. Lower absolute values of cfPWV in this study may result from the younger age of patients compared with those from the former studies, and also from the exclusion of diabetic patients, in whom arterial stiffness is increased compared with nondiabetic dialysis patients.<sup>21</sup>

In another study<sup>10</sup> based on the measurement of baPWV, increased arterial stiffness in HD patients compared with PD patients was observed, despite no significant differences in age, sex, BP, or diabetes prevalence between the study groups. It should be noted, however, that the measurement of baPWV includes both elastic and muscular arteries and thus is a distinct biological parameter. Therefore, baPWV and cfPWV cannot be directly compared, although a significant correlation was found between the results of baPWV and cfPWV measurements.<sup>22</sup> A significant correlation was also observed between these 2 parameters and the severity of left ventricular hypertrophy.<sup>22</sup>

In a study by Mimura et al.<sup>11</sup> with serial baPWV measurements in PD and HD patients, significantly higher values of baPWV were observed in HD patients compared with PD patients after 1-year follow-up, while the baseline values did not differ between the groups. In 2 other studies, parameters of arterial stiffness in PD patients did not

change during 1-year follow-up.<sup>23,24</sup> Lower arterial stiffness in PD patients was associated with preserved residual renal function.<sup>11,25</sup> Increased arterial stiffness in HD patients was also reported by Konings et al.,<sup>26</sup> who showed that arterial distensibility coefficient was decreased in HD, but not PD patients, when compared with control subjects.

Physiological aging leads to several alterations in cells, matrix, and molecules in the arterial wall. These changes may initiate CV diseases and enhance their progression.<sup>27</sup> Arterial stiffness also increases with physiological aging, and age is the main determinant of PWV.<sup>28</sup> Age-induced arterial stiffening is associated with BP changes. Altered age-related BP pattern is recognized as an indicator of accelerated arterial aging.<sup>29</sup> Moreover, PWV is considered as a marker of arterial aging, particularly in those over 50 years of age.<sup>30</sup>

In our study, the value of PWV<sub>M</sub> in PD and HD patients was higher than PWV<sub>T</sub>, calculated based on patients' age, sex, MAP, and heart period. The difference between PWV<sub>M</sub> and PWV<sub>T</sub> was 2.0 m/s, and was statistically significant ( $P < 0.001$ ). From the equation of Blacher et al.,<sup>13</sup> it can be concluded that PWV increases with age by 0.8 m/s for each decade of life. The difference in PWV<sub>M</sub> and PWV<sub>T</sub> of about 2.0 m/s reflects the difference in age of about 25 years. Of note, positive PWV index is associated with unfavorable prognosis in HD patients, and provides information about CV and overall mortality risk.<sup>13</sup>

Our study has several limitations resulting from a small number of patients. Because only a small group of HD patients from a large HD population was recruited for the study, selection bias cannot be excluded. Secondly, the study groups differed significantly with respect to duration of dialysis therapy, which is longer in HD patients. The duration of dialysis therapy is considered one of the factors affecting arterial stiffness in dialysis patients.<sup>11</sup> However, PWV increased with the duration of renal replacement therapy in HD patients,<sup>11</sup> but did not change in PD patients.<sup>11,24</sup> Thus, it can be speculated that arterial stiffness would be higher in PD patients when PD and HD patients with the same duration of dialysis therapy were compared. On the other hand, no correlation was observed between the duration of dialysis therapy and PWV. Several other studies either did not show the relationship between duration of dialysis therapy and arterial stiffness.<sup>4,6,7,13</sup> To investigate this issue further, longitudinal studies in incident PD and HD patients are needed.

Another limitation of our study is that PWV measurements in HD patients were performed before a midweek HD session. In a recent study, in which PWV measurements were performed along 3 consecutive HD sessions and interdialysis periods during week-long period, cyclic changes in PWV values have been observed.<sup>31</sup> The highest value of PWV was observed before the first dialysis in

a week, and a statistically significant reduction in PWV was noted during each session. A significant correlation was found between the change in PWV and ultrafiltration volume during HD session. The results of the study suggest that the most representative time point for PWV measurement in HD patients is the day without HD.<sup>31</sup>

To conclude, arterial stiffness is equally high in PD and HD patients. PWV<sub>M</sub> in both these groups is significantly higher compared with PWV<sub>T</sub>. This finding may reflect accelerated arterial aging.

**Note** The results of the study were presented at XIX Conference of the Polish Society of Nephrology, Rzeszów, June 2–4, 2011 and published as an abstract in *Nefrologia i Dializoterapia Polska*. 2011; 15: 144.

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# Porównanie sztywności tętnic u chorych ze schyłkową niewydolnością nerek leczonych dializą otrzewnową i hemodializą

Paweł Stróżecki, Rafał Donderski, Anna Kardymowicz, Jacek Manitius

Klinika Nefrologii, Nadciśnienia Tętniczego i Chorób Wewnętrznych, Uniwersytet Mikołaja Kopernika, Collegium Medicum im. Ludwika Rydygiera w Bydgoszczy, Bydgoszcz

## SŁOWA KLUCZOWE

dializa otrzewnowa, hemodializa, prędkość fali tętna, sztywność tętnic

## STRESZCZENIE

**WPROWADZENIE** Sztywność tętnic u chorych dializowanych jest zwiększona. Wyniki dotychczasowych badań porównujących sztywność tętnic u chorych dializowanych otrzewnowo (*peritoneal dialysis* – PD) i hemodializowanych (HD) nie pozwalają na wyciągnięcie jednoznacznych wniosków.

**CELE** Celem pracy było porównanie prędkości fali tętna (*pulse wave velocity* – PWV) między chorymi leczonymi PD i HD oraz porównanie wartości zmierzonego PWV ( $PWV_M$ ) z teoretyczną wartością tego parametru ( $PWV_T$ ).

**PACJENCI I METODY** Badaną populację stanowiło 35 chorych leczonych PD oraz 26 chorych leczonych HD, u których przeprowadzono pomiar  $PWV_M$  między tętnicą szyjną i tętnicą udową za pomocą aparatu Complior. U wszystkich chorych obliczono także wartość  $PWV_T$  według równania opracowanego przez Blachera i wsp.

**WYNIKI** Pacjenci nie różnili się znamienne pod względem wieku, płci oraz częstości występowania cukrzycy. Wartości  $PWV_M$  (PD:  $12,1 \pm 3,3$  vs HD:  $12,0 \pm 3,0$  m/s) oraz  $PWV_T$  (PD:  $10,0 \pm 1,4$  vs HD:  $9,9 \pm 1,2$  m/s) nie różniły się znamienne w obu grupach chorych.  $PWV_M$  było znamienne większe niż  $PWV_T$  zarówno u chorych leczonych PD, jak i HD. Ciśnienie tętnicze rozkurczowe i średnie ciśnienie tętnicze były wyższe u chorych leczonych PD, natomiast ciśnienie skurczowe i ciśnienie tętna nie różniły się znamienne w obu grupach. U chorych leczonych PD stosowano większą liczbę leków obniżających ciśnienie tętnicze niż u chorych leczonych HD ( $3 \pm 1$  vs  $2 \pm 1$ ;  $p < 0,05$ ).

**WNIOSKI** Sztywność tętnic jest równie wysoka u chorych leczonych PD i HD.  $PWV_M$  u chorych leczonych PD i HD jest znacznie większa niż  $PWV_T$ , co może wskazywać na przyspieszone starzenie się naczyń tętniczych u pacjentów dializowanych.

### Adres do korespondencji:

dr med. Paweł Stróżecki, Klinika Nefrologii, Nadciśnienia Tętniczego i Chorób Wewnętrznych, ul. M. Skłodowskiej-Curie 9, 85-094 Bydgoszcz, tel.: 52-585-45-51, fax: 52-585-40-30, e-mail: st\_pawel@cm.umk.pl  
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