

# Ankle-brachial index in hemodialysis patients

## *Índice tornozelo-braço em pacientes hemodialíticos*

Mariane Torres Uchôa<sup>1</sup>, Diego Nunes de Albuquerque Oliveira<sup>2</sup>, Maria Eliete Pinheiro<sup>3</sup>, Daniella Bezerra Duarte<sup>4</sup>, Jairo Calado Cavalcante<sup>5</sup>, Glauber Schettino Silva<sup>6</sup>, Marcos Mota Gomes<sup>7</sup>

### Abstract

**Introduction:** Despite the high mortality rates of hemodialysis patients from cardiovascular diseases, diagnostic tests for peripheral arterial occlusive disease (PAOD) and poorly compressible arteries are not routinely performed.

**Objectives:** To analyze the prevalence of peripheral arterial disease and poorly compressible arteries in hemodialysis patients, by comparing them to a Control Group.

**Methods:** This is a cross-sectional study of 78 hemodialysis patients and 88 non-hemodialysis patients with at least two risk factors for peripheral arterial disease (Control Group). Arterial blood pressure of both lower limbs at the ankle was evaluated by portable vascular Doppler and sphygmomanometer. The arterial blood pressure of the upper limb without arteriovenous fistula was measured. The ankle-brachial index was calculated for each artery of the lower limb. Values from 0.9 to 1.3 were considered normal.

**Results:** PAOD and poorly compressible arteries were diagnosed in 26.9 and 30.8% of hemodialysis patients and in 33 and 22.7% of the Control Group. In hemodialysis patients, we found abnormal ankle-brachial index in 75% of symptomatic patients ( $p=0.005$ ), in 67.3% of men and 31% of women ( $p<0.005$ ), in 78.6% of the elderly, 34.8% of young adults ( $p<0.01$ ), and 76.9% of diabetics ( $p<0.005$ ) versus nondiabetics. Peripheral arterial disease was more common among these patients than those from Control Group.

**Conclusions:** Abnormal ankle-brachial index was common in the groups studied; however, hemodialysis patients had more severe alterations when compared to the Control Group. Diabetes mellitus, male gender, and advanced age were important risk factors for abnormal ankle-brachial index in hemodialysis patients. The ABI is a good method for the diagnosis of the studied changes; therefore, we suggest it to be routinely measured in hemodialysis patients.

**Keywords:** ankle-brachial index; dialysis; peripheral vascular diseases.

### Resumo

**Introdução:** Apesar da elevada mortalidade dos pacientes em hemodiálise devido às doenças cardiovasculares, é incomum a realização de exames diagnósticos para doença arterial obstrutiva periférica e artérias pouco compressíveis.

**Objetivos:** Analisar a prevalência de doença arterial obstrutiva periférica e artérias pouco compressíveis em hemodialisados, comparando-os com o Grupo Controle.

**Métodos:** Tratou-se de um estudo transversal, com 78 hemodialisados e 88 pacientes que não faziam hemodiálise com, pelo menos, dois fatores de risco para doença arterial obstrutiva periférica (Grupo Controle). Para aferição da pressão arterial sistólica, utilizou-se Doppler vascular portátil e esfigmomanômetro. Esta foi aferida somente nos membros que não possuíam fístula arteriovenosa. O índice tornozelo-braço foi calculado utilizando cada artéria do membro inferior. Foram considerados normais os valores de 0,9 a 1,3.

**Resultados:** Diagnosticou-se doença arterial obstrutiva periférica e artérias pouco compressíveis em 26,9 e 30,8%, dos hemodialisados, e em 33 e 22,7%, do Grupo Controle. Nos hemodialisados, verificou-se o índice tornozelo-braço alterado em 75% dos sintomáticos ( $p=0,005$ ), em 67,3% dos homens e 31% das mulheres ( $p<0,005$ ), em 78,6% dos idosos, 34,8% dos adultos jovens ( $p<0,01$ ) e em 76,9% dos diabéticos ( $p<0,005$  versus não diabéticos). Esses pacientes apresentaram maior prevalência de doença arterial obstrutiva periférica grave do que o Grupo Controle ( $p<0,01$ ).

**Conclusões:** O índice tornozelo-braço anormal foi muito prevalente nos grupos estudados; entretanto, os hemodialisados apresentaram alterações mais graves quando comparados ao Grupo Controle. Diabetes melito, sexo masculino e idade avançada foram fatores de risco importantes para a alteração do índice tornozelo-braço nos hemodialisados. O índice tornozelo-braço foi um bom método de rastreio para alterações pesquisadas. Portanto, a utilização deste na rotina de manejo de pacientes em hemodiálise é sugerida.

**Palavras-chave:** índice tornozelo-braço; diálise; doenças vasculares periféricas.

From the Hospital Universitário of Universidade Federal de Alagoas, at Clinitor, and at the Hospital Ortopédico de Maceió – Maceió (AL), Brazil.

<sup>1</sup> Physician, Universidade Federal de Alagoas (Ufal) – Maceió (AL), Brazil.

<sup>2</sup> Physician, Universidade Federal de Alagoas (Ufal) – Maceió (AL), Brazil.

<sup>3</sup> Nephrologist; Professor (PhD) at Universidade Federal de Alagoas (Ufal) – Maceió (AL), Brazil.

<sup>4</sup> Nephrologist; Professor at Universidade Federal de Alagoas (Ufal) – Maceió (AL), Brazil.

<sup>5</sup> Physician; Specialist of Epidemiology; Professor (MD) at Universidade Federal de Alagoas (Ufal) – Maceió (AL), Brazil.

<sup>6</sup> Physical Therapist at Centro de Pesquisas Clínicas da Clinitor – Maceió (AL), Brazil.

<sup>7</sup> Cardiologist; Coordinator of the Centro de Pesquisas Clínicas da Clinitor – Maceió (AL), Brazil.

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## Introduction

Despite the high mortality rates from cardiovascular diseases reported in hemodialysis patients, diagnostic tests for poorly compressible arteries and peripheral arterial occlusive disease (PAOD) are not commonly performed, even though these entities are frequent in patients with chronic kidney disease<sup>1-9</sup>. Cardiovascular mortality in hemodialysis patients is 5-30 times higher than in the general population<sup>10</sup>, and PAOD is an independent predictor of heart failure<sup>11</sup>.

Some scientific associations disagree that chronic kidney disease implies PAOD risk<sup>12</sup>, but most authors confirm and emphasize the importance of this relationship<sup>2,13</sup>.

Regardless of the controversy over the classification of chronic kidney disease as a high-risk factor for PAOD, there are very few studies to allow the resolution of this impasse and to evaluate for such diseases in hemodialysis patients. The recommendations for PAOD diagnosis in patients with chronic renal failure by the Kidney Disease Outcomes Quality Initiative (K/DOQI), for instance, are based on studies with pre-dialysis patients and on experts' opinions<sup>1,13</sup>.

Both PAOD and poorly compressible arteries are associated with increased mortality rates (from cardiovascular or other causes) in patients with chronic renal disease<sup>14,15</sup>. In hemodialysis patients, this increase is present even in cases of asymptomatic PAOD<sup>1</sup>. The search for symptoms and pulse palpation in the lower limb arteries are ineffective for the diagnosis of these diseases.

Ankle-brachial index (ABI) is a low-cost and non-invasive method<sup>8</sup> which has 95% sensitivity and 99% specificity for PAOD compared to angiography (gold-standard pattern)<sup>2</sup>. Abnormal ABI values are associated with higher morbimortality rates<sup>7,16</sup>, hence it is considered to be a reliable prognosis predictor. ABI measurement in hemodialysis patients is not routinely performed, so the prevalence of PAOD and poorly compressible arteries are not properly documented.

The aim of this study was to analyze the prevalence of PAOD and poorly compressible arteries in a group of patients on hemodialysis and to compare the findings with a control group at high risk for both diseases. The ABI values were then correlated with risk factors or signs and symptoms found in patients with chronic kidney disease.

## Methods

This was a cross-sectional study conducted with 78 patients on hemodialysis from a public and a private service

of Nephrology, and 88 patients not on hemodialysis from a private service of Cardiology (Control Group).

The hemodialysis group included patients older than 18 years on renal replacement therapy by hemodialysis, patients with a functioning arteriovenous fistula in upper limb, patients that were not on dialysis for acute renal failure and had no amputations of both lower limbs or the upper limb contralateral to the fistula.

The control group included patients older than 18 years with at least two risk factors for PAOD, without amputations of upper or lower limbs, and no fistulas or chronic kidney disease. Patients from three dialysis centers meeting the inclusion criteria were invited to participate in the study. Two patients who refused to be examined, one that complained of severe pain at lower limb blood pressure measurement, and one patient with undetectable blood pressure in the upper limb were excluded from the sample.

The research project was approved by the Ethics Committee of the University to which the study is related (procedure 009707/2010-11). All patients signed an informed consent form before data collection. Demographic data were collected through interviews with individuals in control group, which included questions on drugs taken and presence of comorbidities.

In the hemodialysis group, we collected the same information plus signs and/or symptoms related to PAOD (rest pain, intermittent claudication, signs of hypoperfusion, history of lower extremity revascularization, or amputation and necrosis of the fingers, feet or one of the lower limbs).

Patients whose medical record had the diagnosis of systemic arterial hypertension, those with blood pressure measurement greater than 140 × 90 mmHg on the day of examination, and those using anti-hypertensive drugs were classified as hypertensive<sup>17</sup>.

Patients with diagnosis of diabetes in medical records or in regular use of antidiabetic drugs were classified as diabetics<sup>18</sup>.

After the interview, physical examination was performed and anthropometric data was collected.

The patient was placed in supine position for at least 5 minutes before the hemodialysis session (in the case of Hemodialysis Group) in order for the systolic blood pressure of the lower limbs' arteries (posterior tibial and dorsalis pedis arteries) to be measured, as well as both upper limbs' arteries (Control Group) or only the limb that was contralateral to the arteriovenous fistula (hemodialysis patients).

Systolic blood pressure was measured twice in each artery by different examiners previously trained, using portable vascular Doppler ultrasound (model DV-

2001, Medpej® in São Paulo, Brazil) and a calibrated sphygmomanometer (aneroid mechanical model, BD®, Germany).

The ABI was obtained by simple division of the higher systolic blood pressure obtained in each artery of the lower limb by the values obtained in the upper limbs (Control Group) of those not presenting arteriovenous fistula (hemodialysis patients).

In order to increase the method's sensitivity, up to two ABI values were obtained from each lower limb of each patient. The indexes were then included in the database, because considering only the highest blood pressure values in a certain extremity would underestimate the poorly compressible arteries, since some patients present both alterations in the same limb.

ABI was considered abnormal when lower than 0.9 (indicative of PAOD)<sup>1-3,8,11,15,19-26</sup> or higher than 1.3 (indicative of poorly arterial compressibility)<sup>1,3,8,19,25</sup>. ABI between 0.7 and 0.9 were considered to indicate mild PAOD; between 0.4 and 0.7, moderate PAOD; and below 0.4, severe PAOD<sup>24</sup>.

Poorly compressible arteries were those that could not be compressed, that is, not showing bruit fading (Korotkoff Phase V), even when inflating the cuff at 300 mmHg.

Arteries with inaudible signals were those that could not be identified by portable vascular Doppler ultrasound performed by both examiners.

After gathering of information and patients' examination, the data was typed in a database program (Epi-Info Windows, version 3.4.3) for statistical analysis.

Qualitative variables were measured by the  $\chi^2$  test and Odds Ratio.

Numerical variables were assessed by means of ANOVA test and showed the rang homogeneity by Bartlett's test. Afterwards, the non-parametric Kruskal-Wallis test was used when necessary.

The results with error probability inferior to 5% ( $p < 0.05$ ) were considered statistically significant.

**Results**

In the hemodialysis group, mean age was  $49.07 \pm 14.89$  (mean  $-X \pm$  standard deviation  $- SD$ ) and mean time on dialysis was  $36.90 \pm 35.65$  months ( $X \pm SD$ ).

Males and caucasian patients were more common in the dialysis group, with 49 and 34, respectively. This group had 76 (97.4%) patients with hypertension, 10 (12.8%) smokers, 11 (14.1%) former smokers and 24 (30.8%) patients with coronary disease.

In the control group, the mean age was  $61.09 \pm 12.07$  years, and there were 52 (59.1%) male patients, 42 (47.7%) caucasians, 57 (64.8%) patients with hypertension, 14 (15.9%) smokers, 34 (38.6%), former smokers and 54 (61.4%) patients with coronary artery disease, which characterizes a group at high risk for peripheral arterial disease.

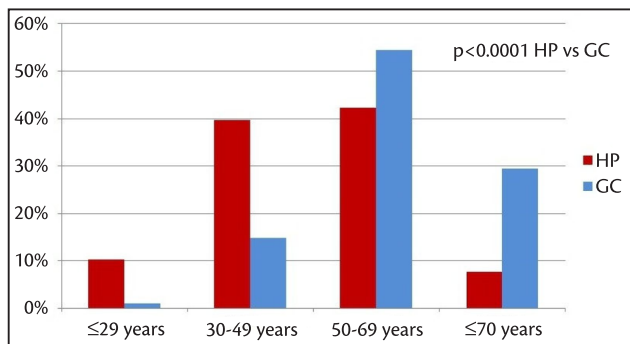
The prevalence of diabetes mellitus and cerebrovascular diseases were similar in both groups, which allocated nine patients with cerebrovascular disease and a similar number of diabetic patients: 26 in the hemodialysis group and 25 in the control group.

Systolic blood pressure measurements were higher than the values recommended by the Brazilian Society of Hypertension<sup>17</sup> (Table 1).

Age groups showed to be statistically significant in the analysis, as shown in Figure 1.

Twenty-eight patients on hemodialysis (35.9%) presented the signs and/or symptoms searched for; however, only 12 (42.9%) patients had an ABI < 0.9, and 11 (39.3%) had an ABI > 1.3. Twenty-one (75%) symptomatic patients had abnormal ABI, with a relative risk of 1.79 ( $p = 0.005$ ).

Five patients who had tissue necrosis or amputation of fingers, feet or limbs (6.4% of hemodialysis patients) had abnormal ABI ( $p < 0.05$ ), and no patient reported history of peripheral revascularization.



HP: hemodialysis patients; GC: Control Group.

**Figure 1.** Distribution of patients according to age group.

**Table 1.** Systolic blood pressure values and ankle-brachial index in hemodialysis and control patients

Variables	HP	Control Group	P value
BP UL – mmHg	155.79±29.21	144.13±25.64	0.007 <sup>a</sup>
BP RUE – mmHg	181.11±61.50	155.26±38.91	0.001 <sup>k</sup>
BP RLE – mmHg	177.9±53.82	151.01±32.19	0.000 <sup>k</sup>
ABI RLE	1.17±0.37	1.09±0.26	0.066 <sup>k</sup>
ABI LLE	1.15±0.90	1.06±0.50	0.014 <sup>k</sup>

HP: hemodialysis patients; BP: blood pressure; ABt: ankle-brachial index; UE: upper extremity; RLE: right lower extremity; LLE: left lower extremity; <sup>a</sup>ANOVA test; <sup>k</sup>Kruskal-Wallis test; results expressed in mean±standard deviation.

In addition, 21 patients (half of the hemodialysis group) presenting abnormal ABI were asymptomatic, and eight of them presented ABI < 0.9.

No statistical difference was found as to the prevalence of altered ABI between the groups, although poorly compressible arteries were more prevalent in patients on hemodialysis, and PAOD affected more patients in the control group (Table 2).

Figures 2 and 3 show that the most significant alterations affected more patients from the hemodialysis group than those from the control group. Thus, no subjects in the control group showed ABI < 0.4, while 29% of patients on hemodialysis with PAOD (6 patients) had a more severe form of the disease.

More than half of the patients diagnosed with PAOD in the control group had the disease in its mild form (25 patients), whereas only 15 patients in the hemodialysis group were classified as such.

Also, 10 (23.8%) hemodialysis patients with abnormal ABI had poorly compressible arteries *versus* 3 (6.8%) from the other group presenting altered ABI and relative risk of 3.49 (p<0.05).

No patient in the control group presented inaudible arterial flow, while this finding was observed in 7 (16.7%) hemodialysis patients with abnormal ABI (p<0.005).

As one may note from Figure 4, altered ABI was more common among males than females in both groups, but

only the hemodialysis group was found to be statistically significant as to this difference (p<0.005), where ABI was abnormal in 33 men and 9 women, with a relative risk of 1.77.

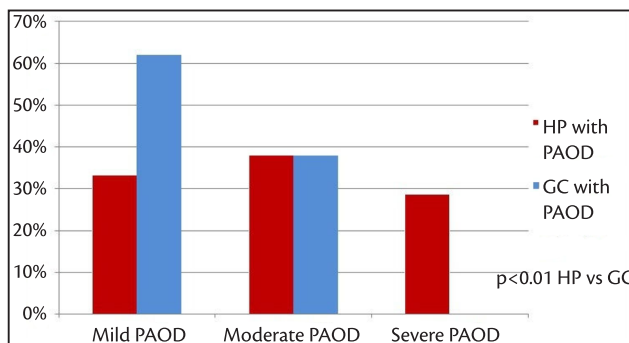
In the group of patients on hemodialysis, a statistically significant difference was observed in elderly and young adults with altered ABI (p <0.01), unlike the control group, in which only four individuals were considered to be young adults. Out of the 14 elderly patients in the hemodialysis group, 11 (78.6%) had abnormal ABI, as well as 8 out of the 23 young adults in this group (34.8%).

Thus, patients over 65 years of age were found to be more likely to present abnormal ABI compared to those aged 20 to 39 years and relative risk of 2.26.

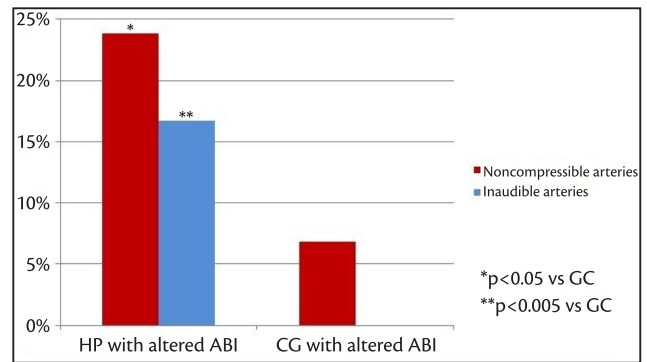
**Table 2** - Prevalence of normal and abnormal ABI values

ABI interpretation	HP (n - %)	Control Group (n - %)	P value
Normal ABI	36-46.2	44-50.0	NS
PAOD	21-26.9	29-33.0	NS
Poorly compressible arteries	24-30.8	20-22.7	NS
Both alterations	3-3.8	5-5.7	NS

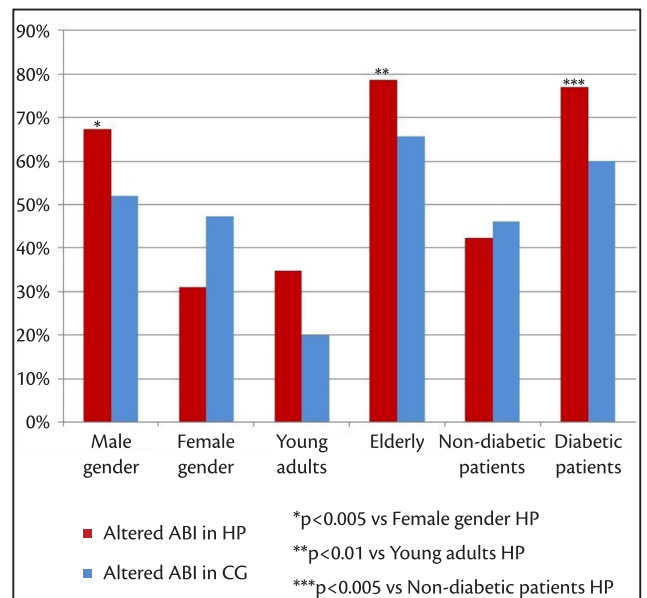
HP: hemodialysis patients; ABI: ankle-brachial index; PAOD: peripheral arterial occlusive disease; NS: non significant; \* $\chi^2$  test.



PAOD: peripheral arterial occlusive disease; HP: hemodialysis patients; GC: Control Group. **Figure 2.** Degrees of PAOD in hemodialysis and control patients.



HP: hemodialysis patients; CG: Control Group; ABI: ankle-brachial index. **Figure 3.** Prevalence of noncompressible and inaudible arteries in hemodialysis and control patients.



HP: hemodialysis patients; CG: Control Group; ABI: ankle-brachial index. **Figure 4.** Distribution of risk factors and variables corresponding to hemodialysis and control patients with altered ABI.

Another important risk factor analyzed is diabetes mellitus. The prevalence of alterations in ABI among diabetic patients is higher than that of non-diabetics, a statistically significant relation in the hemodialysis group ( $p < 0.005$ ). In this group, 20 (76.9%) patients with diabetes presented abnormal ABI, with a relative risk of 2.86.

The diabetic patients of both groups showed a prevalence of poorly compressible arteries slightly higher than individuals without the disease, but only in hemodialysis patients were considered statistically significant as to this feature ( $p < 0.01$ ). Therefore, seven patients on hemodialysis with poorly compressible arteries were identified.

Among patients included in an hemodialysis program for up to five years, the frequency of abnormal ABI increased gradually. From this period on, a decrease of this frequency was noted.

Thus, we found alterations in ITB in 51.6% of patients on hemodialysis for up to one year, in 60% of patients on the program for one to three years, in 64.3% those being treated for three to five years, and in 50% of patients on hemodialysis for more than five years.

## Discussion

The predominance of males in the hemodialysis group was similar to that of other studies conducted with patients undergoing hemodialysis<sup>1,10,14</sup>, but it differs from findings in studies with pre-dialysis patients<sup>19</sup>. One explanation for this is that men go on to stage 5 of chronic kidney disease more often than women, in which the estrogen hormone functions as protective factor, favoring angiogenesis and slowing the progression of the disease to the terminal stage<sup>27,28</sup>.

Smoking, male gender, diabetes mellitus, advanced age, coronary and cerebrovascular diseases are risk factors for ABI alterations and high mortality<sup>1,6,9,14</sup>. As indicated, the prevalence of these factors in patients from the control group was higher than in the hemodialysis group, which sets up a group at high risk for PAOD.

The high prevalence of hypertension and diabetes mellitus in patients undergoing hemodialysis, which is compatible with the findings of studies by Ono et al.<sup>14</sup> and Longenecker et al.<sup>10</sup>, was expected because these are the leading causes of chronic kidney disease<sup>29</sup>, besides being the most common chronic degenerative diseases in Brazil.

The common finding of abnormal ABI in both groups, even though no statistical difference has been found between them and the control group has presented more risk factors, demonstrates that end-stage chronic kidney disease is an important risk factor for altered ABI,

which was also observed by De Loach and Mohler<sup>1</sup> and is highlighted in the K/DOQI guidelines<sup>13</sup> and Transatlantic Inter-Society Consensus Document on Management of Peripheral Arterial Disease (TASC II)<sup>2</sup>.

Liew et al.<sup>24</sup> stated that patients with chronic kidney disease and PAOD are at a significantly higher risk of death than patients with either disease alone. This finding justifies the continuous searching for PAOD diagnosis and poorly compressible arteries in patients on hemodialysis.

The inclusion of end-stage chronic kidney disease as a significant risk factor for cardiovascular diseases can be explained both by the traditional and nontraditional cardiovascular risk factors, the latter acting the development of atherosclerosis. Among the traditional risk factors, the most common are diabetes, hypertension, sedentary lifestyle, hypertriglyceridemia, smoking, and low HDL, the former being the most significant factor related to the onset of cardiovascular diseases and PAOD<sup>1,10,30-33</sup>.

As it was noted, eight hemodialysis patients who were diagnosed with PAOD by ABI were asymptomatic, which proves the efficacy of ABI in PAOD diagnosis compared to the method used as routine in clinical practice for this purpose (search for symptoms and pulses of lower limb arteries). Moreover, it makes one reflect on the large number of patients with PAOD that go unnoticed in hemodialysis services that do not measure ABI routinely.

A high prevalence of asymptomatic patients with abnormal ABI was also described by O'Hare<sup>3</sup>, Carmo et al.<sup>19</sup> and Makdisse et al.<sup>11</sup>, which underscores the importance of ABI as a method for PAOD diagnosis.

Seven symptomatic patients on hemodialysis (25%) had normal ABI. However, patients presenting with tissue necrosis or that had been submitted to some type of amputation had alterations on ABI.

The high rate of amputations in hemodialysis patients is attributed to chronic kidney disease and to the high prevalence of diabetes mellitus<sup>1,2,34</sup>. The absence of ABI measurement in patients at the services included in this study is another factor contributing to high amputation rates.

As expected, old age increased the risk of abnormal ABI in both groups, but most frequently among hemodialysis patients. The studies of Ono et al.<sup>14</sup>, De Loach and Mohler<sup>1</sup>, Cheung et al.<sup>6</sup> and Resnick et al.<sup>15</sup> also showed that advanced age and the presence of diabetes mellitus are associated with alterations in ABI.

After the fifth year of hemodialysis, a decrease in the prevalence of the studied variables was observed. This may be related to the high mortality rates in this population, which is in agreement with De Loach and Mohler<sup>1</sup>, Sesso<sup>35</sup>

e Silva et al.<sup>36</sup>, which state that the probability of survival in diabetic patients undergoing hemodialysis for more than five years are 25%, 23% and 50%, respectively<sup>1,35,36</sup>.

The prevalence of PAOD in hemodialysis patients was 26.9%, and is in agreement with the findings by O'Hare<sup>3</sup>, which states that this value varies from 12 to 32%.

In the hemodialysis group, 30.8% of patients had poorly compressible arteries, a value slightly higher than those found by a Finnish study, in which the prevalence of poorly compressible arteries was estimated to be 24%<sup>3</sup>.

The higher prevalence of poorly compressible arteries among hemodialysis patients is consistent with data presented by Ono et al.<sup>14</sup> and is attributed to the fact that patients with end-stage renal disease have secondary severe bone dystrophy<sup>7,37,38</sup>. The authors suggest that the prevalence of PAOD is likely to be underestimated, for patients with poorly compressible arteries may present it regardless of abnormal ABI<sup>25</sup>.

Patients in the group of hemodialysis presented with more severe disease compared to those in the control group, as the latter did not present inaudible arteries or severe PAOD. This is very important data, as ABI < 0.5 in symptomatic patients is a strong predictor of amputation<sup>2</sup>.

## Conclusions

PAOD and poorly compressible arteries were frequent findings in both groups. However, hemodialysis patients presented with more severe alterations such as noncompressible or inaudible arteries, or amputation, even when compared with patients who were not on hemodialysis but presented risk factors, i.e. advanced age, smoking and coronary heart disease.

Abnormal ABI in hemodialysis patients, whether indicating PAOD or poorly compressible arteries, was strongly correlated with the variables: male gender, diabetes and advanced age. In half of patients diagnosed with PAOD by ABI, the disease was asymptomatic, so the use of this index as a method of search for vascular alterations should be considered. Therefore, we suggest the use of ABI in the routine assessment of patients undergoing hemodialysis.

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**Correspondence:**

Mariane Torres Uchôa  
Loteamento Jardim Petrópolis I, quadra CH, 207 – Jardim Petrópolis  
CEP: 57080-535 – Maceió (AL), Brazil  
E-mail: [marianeuchoa@gmail.com](mailto:marianeuchoa@gmail.com)

**Authors' contribution**

Study conception and design: MTU, DNAO, MEP, DBD  
Data analysis and interpretation: MTU, DNAO, MEP, JCC  
Data collection: MTU, DNAO, GSS  
Writing: MTU, DNAO, MEP  
Critical analysis: MTU, DNAO, MEP, MAMG  
Final approval\*: MTU, DNAO, MEP, DBD, JCC, GSS, MAMG  
Statistical analysis: MTU, DNAO, JCC  
Overall responsibility: MEP

\*All authors have read and approved the final version of the paper submitted to J Vasc Bras.