Value of doppler ultrasonography in the study of hemodialysis peripheral vascular access dysfunction

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Abstract

Objective: The main objectives of this study were to evaluate the sensitivity and specificity of duplex Doppler ultrasonography in the study of hemodialysis peripheral vascular access dysfunction and to analyze the resistance index and flow in the afferent artery.

Materials and methods: We prospectively studied 178 patients with 178 peripheral vascular accesses that were dysfunctional in at least three consecutive hemodialysis sessions. Patients underwent duplex Doppler ultrasonography and clinical and laboratory follow-up for three months (provided angiography findings were negative). We calculated the sensitivity, specificity, predictive values, and coefficients of probability. We studied the morphology of the afferent artery, the arteriovenous anastomosis, and the efferent vein, and we measured the resistance index and the flow of the afferent artery, the diameter of the anastomosis, and the flow and peak systolic velocity in the efferent vein.

Results: The final sample consisted of 159 patients. The sensitivity, specificity, positive and negative predictive values, and positive and negative coefficients of probability were 0.98 (95% CI: 0.88–1.00), 0.74 (95% CI: 0.66–0.81), 0.96, 0.82, 3.7, and 0.03, respectively. The resistance index was less than 0.5 in 78.5% of the peripheral vascular accesses with normal function and greater than 0.5 in 86.1% of the dysfunctional peripheral vascular accesses. We found aneurysms in 19 of the native peripheral vascular accesses and pseudoaneurysms in 7 of the prosthetic grafts. Inverted flow was seen in 57 peripheral vascular accesses.

Conclusion: Duplex Doppler ultrasonography is an efficacious method for detecting and characterizing stenosis and thrombosis in peripheral vascular accesses, and it provides information about the morphology and hemodynamics.

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PALABRAS CLAVE
Ecografía; Estudios doppler; Accesos de hemodiálisis; Acceso vascular; Estenosis de fistula arteriovenosa; Métodos de vigilancia

Valor de la ecografía doppler en la disfunción de los accesos vasculares periféricos para hemodiálisis

Resumen

Objetivo: El objetivo principal del estudio es evaluar la sensibilidad y especificidad de la ecografía dúplex-Doppler para estudiar la disfunción de los accesos vasculares periféricos para hemodiálisis, y analizar el índice de resistencia y el flujo en la arteria aferente.

Material y métodos: Se estudiaron prospectivamente 178 pacientes con 178 accesos vasculares periféricos disfuncionantes durante al menos 3 sesiones de hemodiálisis seguidas. Se realizaron ecografía dúplex-Doppler, angiografía y seguimiento clínico y analítico durante 3 meses (si la angiografía fue negativa). Se calcularon los valores de sensibilidad, especificidad, valores predictivos y cocientes de probabilidad. Se estudiaron morfológicamente la arteria aferente, la anastomosis arteriovenosa y la vena eferente, y se midieron el índice de resistencia y el flujo de la arteria aferente, el diámetro de la anastomosis, y el flujo y velocidad pico sistólica en la vena eferente.

Resultados: La muestra final la constituyeron 159 pacientes. Los valores de sensibilidad, especificidad, valor predictivo positivo y negativo y cociente de probabilidad positivo y negativo, fueron 0,98 (IC 95% 0,88–1), 0,74 (IC 95% 0,66–0,81), 0,96, 0,82, 3,7 y 0,03 respectivamente. El índice de resistencia fue <0,5 en el 78,5% de los accesos vasculares periféricos normo funcionantes y >0,5 en el 86,1% de los disfuncionantes. Se encontraron aneurismas en 19 de los accesos vasculares periféricos nativos y seudoaneurismas en 7 de los protésicos. El flujo invertido apareció en 57 accesos vasculares periféricos.

Conclusión: La ecografía doppler dúplex es un método eficaz de detección y caracterización de estenosis y trombosis del acceso vascular periféricos y aporta información morfológica y hemodinámica.

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Table 1  Epidemiological data and features of peripheral vascular access.

<table>
<thead>
<tr>
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<th>Frequency</th>
<th>Percentage</th>
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<tbody>
<tr>
<td><strong>Epidemiological data</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>36</td>
<td>23.8</td>
</tr>
<tr>
<td>Artery high blood pressure</td>
<td>135</td>
<td>84.9</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>63</td>
<td>39.6</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>46</td>
<td>28.9</td>
</tr>
<tr>
<td>Antiaggregant agents</td>
<td>138</td>
<td>86.79</td>
</tr>
<tr>
<td><strong>Type of vascular access</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internal</td>
<td>127</td>
<td>80.2</td>
</tr>
<tr>
<td>Arteriovenous fistula</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Teflon (polytetrafluoroethylene)</td>
<td>32</td>
<td>19.8</td>
</tr>
<tr>
<td>Left</td>
<td>112</td>
<td>70.4</td>
</tr>
<tr>
<td>Right</td>
<td>47</td>
<td>29.3</td>
</tr>
</tbody>
</table>

To be part of our sample patients had to (1) present alterations of at least 3 back-to-back hemodialysis sessions: reduced kinetic values during dialysis (blood flow \([Q_b]\) < 300 ml/min, urea distribution volume [recirculation] > 10%, reduction > 25% of flow percentage), difficulty in PVA cannulation, prolonged bleeding after hemodialysis, high venous pressures and/or limb edema, and (2) meet all inclusion criteria and no preclusion criteria.

To be included patients needed to undergo a PVA-based hemodialysis, be 18–95 years of age, have undergone ultrasound and angiographic studies for the assessment of PVA and to have signed an informed written consent to be able to participate in the study. Preclusion criteria were the suspicion of iodinated contrast allergy, confirmed or unconfirmed pregnancy, functional PVA but substitute therapy different than hemodialysis, have undergone surgical procedure/s to maintain or reestablish PVA before carrying out the diagnostic radiological studies and hemodialysis performed through a central venous catheter. Withdrawal criteria were the reversal of informed consent at any time of the study, death, or transfer. Fourteen patients were precluded since it was not possible to perform diagnostic proceedings: 6 patients due to the PVA clinical thrombosis needing surgical thrombectomy (n = 4) or the placement of a central catheter (n = 2), and 8 due to loss in the follow-up (transfer to other institution n = 5; death n = 2; and unknown n = 1). Five patients did not give us their informed consent to be part of the study.

**Study modalities and data mining**

The DDU was performed by a 10+ year experienced radiologist in interventional vascular radiology in DDU always before the angiography. The DDU was performed with a Toshiba SSH-140 Doppler duplex scan kit (Toshiba Medical System Corporation, Shimoishigami, Otawara-shi, Japan) in 35 patients and a Toshiba apio XV kit (Toshiba Medical System Corporation, Shimoishigami, Otawara-shi, Japan) in 124 patients. In both cases a linear probe with frequencies between 6 and 12 MHz was used.

The studies were performed with the patient in the supine decubitus position, which brings the explorer close to the PVA limb to first assess the afferent arteriole in mode B, the arteriovenous anastomosis and the efferent vein (Fig. 1) and to later perform the DDU used to study the afferent arteriole RI (after obtaining the peak systolic velocity (PSV) and the end diastolic velocity), the flow of the afferent arteriole (ml/min), the diameter of anastomosis (mm), the flow (ml/min) and the PSV of efferent vein (cm/s) (Fig. 2). The estimation of flow both in the afferent arteriole and in the arterialized vein was done using this formula:

\[
\text{Flow} = \text{time} \times \text{curve-velocity (average of 4 cardiac cycles)} \times (\text{cm/s}) \times 60
\]

Ultrasound criteria of stenosis include: (1) the vessel lumen stenosis was beyond 50% with respect to the adjacent vascular segment with or without the perivascular color artifact, (2) aliasing and (3) one PSV 2 times the PSV of the non-stenotic adjacent vascular segment (Figs. 3 and 4). Spectra were obtained through an ultrasound angle of incidence ≤60. Blood flow was analyzed in the non-stenotic straight segments of the PVA artery after doing measurements after obtaining the average velocity in ml per minute. PSV, the end diastolic velocity and RI were measured in the afferent arteriole (brachial and radial arterioles) 5 cm before anastomosis. The flow from efferent vein was obtained in those accesses with straight segment of uniform diameter at least in 10 cm of non-turbulent unidirectional flow and possibility of insonation with an angle <60°.

![Figure 1](image.png)  
*Figure 1  Vascular access with functioning polytetrafluoroethylene (PTFE) prostheses and no ultrasound alterations. Both anastomoses–proximal to the efferent vein (V, efferent vein) and distal to the brachial artery (dotted line). The PTFE prosthesis whose wall can be seen with a triple band with a hypoechoic central line shows some irregularities secondary to repeated punctures.*
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The angiography was performed just a week after the DDU without knowing its result. The images were assessed by a 10+ year experienced radiologist in interventional vascular radiology. The proceeding was carried out with one Artis Zee digital angiography device (SIEMENS Medical Systems, Erlangen, Germany) by introducing a 20-gauge cannula into PVA of the venous branch or into the Teflon (PTFE) together with anastomosis. The contrast agent used was lohexol 300 mg/ml at a 3–4 ml/s flow with a 2–5 s-injection time and the whole venous outflow tract was initially examined. Then to assess anastomosis and the efferent vein segment proximal to puncture the pressure cuff was compressed while the contrast media agent was administered. Significant stenosis is defined as reductions in the caliber of the efferent vein >50% with respect to the nonaneurysmal venous segment.\textsuperscript{11,12}

PVAs without ultrasound or angiographic alterations were followed both analytically and hemodynamically in hemodialysis sessions during the next 3 months. We tagged

![Image]

**Figure 2** Measurement of flow and RI in the afferent arteriole of a normofunctioning peripheral vascular access. The afferent arteriole is studied with an ultrasound incidence angle <60° to obtain a 4 cycle-range. By knowing the average vessel velocity and area (in the cut that runs perpendicular to its axis) the software of the ultrasound kit gives us the flow (ml/min). RI < 0.5 and the shape of the curve indicate that this is a low-resistance artery.

![Image]

**Figure 3** Stenosis in a peripheral vascular access for hemodialysis. (a) Arteriography. Significant stenosis of efferent vein (*). Juxta-anastomotic stenosis of efferent vein followed by filiform stenosis (white arrow) located some inches away from anastomosis (open arrow). Radial artery (arrow head). (b) The same finding can be seen in the mode B-ultrasound. (c) When placing the mouse pointer on the stenosis we can see a high-speed wave with turbulent flow. (d) A high RI and a change in the curve of velocities of the afferent arteriole (radial artery) with elevated systolic peak velocity and low diastole suggest stenosis.
odds ratio of DDU. True positives were PVAs with alterations (stenosis or thrombosis) in DDU and angiography while true negatives were PVAs without lesions in both assays and without clinical or analytical alterations in the hemodialysis sessions 3 months after the angiography. False positives were PVAs with abnormal DDU but without angiographic alterations even in the follow-up during hemodialysis. False negatives were PVAs with normal DDU showing lesions in the angiography.

RI and flow results were expressed as absolute values with respect to the total and as the average standard deviation.

Results

A hundred and forty of the 159 PVAs studied through angiography showed dysfunction. Nineteen PVAs were normal in the angiography and did not show hemodynamic or analytical alterations in the follow-up during the next 3 months. DDU diagnosed 14 of these PVAs as normal while erroneously diagnosed 5 as not normal after considering there was stenosis in the surgical anastomosis or in the adjacent segment of the efferent vein. DDU categorized 142 PVAs as not normal 5 of which did not show alterations in the subsequent angiography or during the clinical follow-up. Among the 137 PVAs with ultrasound and angiographic dysfunctions 19 were thrombosis (all diagnosed through DDU) and 118 stenoses. Three PVAs were diagnosed as normal in the DDU while the angiography later showed stenosis. In one of the cases post-surgical fibrosis and calcifications produced important perivascular artifacts that did not allow us to measure accurately the diameter of vascular structures and flow velocities. The remaining 2 false negatives were central stenoses (3 stenoses in 2 patients) where the overlapping of bone structures did not allow us to see the veins directly—2 of them affecting the central veins and the other one a proximal segment (proximal third of the arm) of the efferent vein. The DDU sensibility was 0.98 (95% CI 0.88–1), specificity 0.74 (95% CI 0.66–0.81), the positive predictive value 0.96 and the negative predictive value 0.82, the positive odds ratio 3.70 and the negative odds ratio 0.03.

The afferent arteriole RI and flow values are shown in Table 2. We can see a higher flow in the brachial artery with

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Resistance indexes and flow velocity reported in peripheral vascular accesses.</th>
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<tbody>
<tr>
<td>DDU Outcome</td>
<td>n</td>
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<tr>
<td>-----------</td>
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</tr>
<tr>
<td>Without alterations</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombosis</td>
<td>19</td>
</tr>
<tr>
<td>Stenosis</td>
<td>118</td>
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AB: brachial artery; RA: radial artery; DDU: duplex-Doppler ultrasound.

a In 2 patients the flow was maintained >500 ml/min due to the outflow running through collateral veins with proximal birth to the occlusion.
Figure 5  Double color phenomenon. Cuts (a) longitudinal and (b) transversal. Evident separation in the direction of flows in one dilated venous segment; centrifetal flow in red and inverted centrifugal flow in blue.

respect to the radial artery both in the accesses with steno-
sis and in those with no alterations at all. Flow in radial
artery is usually underestimated since the supplementary
flow from collaterals of the palmar arcade is not measured.\textsuperscript{13} 
RI was \( > 0.6 \) in all cases of access thrombosis and \( > 0.5 \) in 99
of the 118 accesses with stenosis. Flow of the efferent vein
could only be measured reliably in 54 of the 159 accesses
due to the presence of inverted flow \( \left( n = 57 \right) \), turbulent flow
\( \left( n = 8 \right) \), lack of pre-bifurcation straight segment \( \left( n = 12 \right) \) or
insonation angle \( > 60 \) \( \left( n = 28 \right) \). Among 14.9\% of native PVAs we
found aneurysms \( \left( 19 \text{ patients} \right) \); 4 PVAs without alterations, 13
PVAs with stenosis and 2 cases of thrombosis). The findings
were: luminal ectasia \( \left( \text{venous diameter} > 12 \text{ mm} \right) \), turbulent
local flow and partial or total mural thrombosis \( \left( \text{in the case}
of 2 aneurysms located in the thrombosed PVAs} \right) \). Among the
32 PVAs with prosthesis 7 PVAs showed pseudoaneurysms \( \left( 2
\text{ in PVAs without alterations and 5 in PVAs with stenosis} \right) \) seen
as secular formations with flow in the DDU linked to the
PTFE. Five of the 26 aneurysms and pseudoaneurysms could
not be seen through the fistulography–3 pseudoaneurysms
and 2 aneurysms. In 35.8\% of the PVAs studied \( \left( n = 57: 9
\text{ PVAs without alterations and 48 PVAs with stenosis} \right) \) besides
the centrifetal flow we also observed an inverted retro-
grade flow depicted on the DDU as areas of different color
(Fig. 5).

Discussion

Most cases of PVA thrombosis are associated with progres-
sive subintimal hyperplasia of venous walls or with the
arteriovenous anastomosis causing stenosis in different
sites of the PVA.\textsuperscript{14} Angiography is still considered the
standard of reference to find these stenoses and further
therapy is through angioplasty or surgery. Yet despite the
fact that it is an invasive modality that uses iodinated
contrast and ionizing radiations it is still used as the early
assay of diagnosis in PVAs with suspicion of dysfunction.
However our study showed that the DDU is a useful assay of
high sensibility and positive predictive value.

The sensibility of the physical exam is good \( \left( 85\% \right) \) for
the diagnosis of anastomotic or juxta-anastomotic stenoses
(inflow) with moderate specificity \( \left( 71\% \right) \) and positive
and negative predictive values of 84\% and 72\% respectively.\textsuperscript{15,16}
As opposed to it our results with DDU are superior showing
a 98\% sensibility and a 96\% positive predictive value while
studying vessels, locating stenosis and measuring diameters.
Since this is a high-prevalence process within the population
with end-stage renal disease in hemodialysis\textsuperscript{5,17} this positive
predictive value almost confirms the condition when ultra-
sounds are positive. The high-positive odds ratio \( \left( 3.70 \right) \) of
our study confirms its validity as a diagnostic test to detect
stenoses and thromboses.

However specificity has only been moderate \( \left( 74\% \right) \)
and stands in contrast to the 98\% reached in other
investigations.\textsuperscript{18} One reason can be the difficulty in transmit-
ting ultrasound through the edema and post-surgical fibrosis
and the other the overestimation of stenosis in the anas-
tomosis due to the artery physiological narrowing after the
surgical proceeding\textsuperscript{10,19} or the difficulty for the ultrasound
incidence angle to be adequate given the small amount of
subcutaneous cellular tissue in the wrist which prevents us
from taking exact measurements of velocities \( \left( 3 \text{ false posi-
tives on radiocephalic native PVAs} \right) \). The information bias
was introduced because the radiologist knew that patients
who had been referred after showing alterations of PVA
might have contributed to the elevated number of false
positives.

The sensibility and specificity of DDU in the diagnosis of
thrombosis is 100\% and its utility is not only diagnostic since
it is far more efficient in the location of the segment of
the patolximal efferent vein and the stenosis responsi-
ble for thrombosis. When the proximal drainage vein is not
patent and size is inadequate thrombectomies, angioplasties
or revascularization surgeries cannot be performed and
therefore the PVA is not recoverable.\textsuperscript{20}

Elevations of RI have been reported in PVAs with steno-
sis or thrombosis. These elevations are associated with
changes in the wave shape and reductions of flow in the
PVA. According to the recommendations by the National
Kidney Foundation Disease Outcomes Quality Initiative\textsuperscript{2}
the reduction of flow is considered today as the most
reliable measure of PVA dysfunction\textsuperscript{10,19,21}. The normal
flow intervals \( \left( 1053 \pm 495 \text{ ml/min with ultrasound dilu-
tion modalities} \right) \textsuperscript{10,19,22} \) and \( 1034 \pm 527 \text{ ml/min with catheter
thermodilution} \textsuperscript{23} \) are widely varied.

Most authors perform ultrasound measurements of the
efferent vein flow which often leads to imprecise and very
variable measurements not associated with the measurements obtained by other modalities. The tortuosity of venous vein, the wide variations in diameter, how easy the ultrasound probe compresses itself and hemodynamic features (the velocity of blood flow in the efferent vein is not even, it does not show parabolic flow and the curve of velocities as a wide range of frequencies) are the causes of such inaccuracy. On the contrary the diameter of the afferent arteriole is constant, its course is always, the spectral curve is clean and flow is parabolic which allows us to perform accurate measurements of flow. After performing a PVA the brachial artery increases its flow progressively while staying in values of 1000 ± 200 ml/min. These values are similar to those of our study in normofunctioning PVAs and they are also similar to values measured through saline dilution and thermodilution. In PVAs with stenosis and/or thrombosis flows grow smaller. In our sample 28.5% of normofunctioning PVAs showed flows <800 ml/min while 10.1% of dysfunctional PVAs showed normal flow (>800–1000 ml/min). From this we deduce the importance of correlating flow values and other hemodynamic data like the wave morphological changes and RI. Flow increases in the PVA can be associated with increases of venous pressure non-attributable to stenosis in the outflow. Similarly the elevations of flow with constant peripheral diameter and resistances could raise velocities and increase the RI (Poiseuille’s law). In our opinion it is flow reductions together with RI elevations that are the ones that would more likely be associated with dysfunctions (stenosis and thrombosis). Because there were few normofunctioning PVAs in our sample we did not establish cutoff values for the flow or IR and did not do a ROC curve analysis either—all to be done in future studies.

The PVA morphological alterations and local complications non-associated with flow or dysfunction are (precluding infectious complications) hematomas and aneurysms and pseudoaneurysms adjacent to the native or prosthetic venous branch of the PVA.

The factors associated with the appearance of aneurysms are repeated punctures, excessive flow distension in the PVA and overpressure in venous segments distal to one stenosis. Both the sensibility and specificity of ultrasounds are high to detect these complications that are even higher than the sensibility and specificity of angiographies due to its ability to detect intraluminal repletion defects and hematomas. In our study we found aneurysms in the ultrasound that went misdiagnosed in the angiography that studies the central residual lumen while overlooking the mural thrombus that takes up a space >50% of the lumen of the affected vessels (19.2% of cases).

In a high percentage of our PVAs there were segments with inverted flow or double color. Inversion can be explained by the Venturi effect and Bernoulli’s equation (Fig. 6). When one vessel widens suddenly—common finding in post-stenotic segments or in one aneurysmal venous segment—the very profile of flow changes, and it lengthens to go back to the parabolic profile. During this process the central blood layer (post-stenotic jet) overcomes cohesion among blood layers. Flow then “splits itself” into slow peripheral flow and high pressure and into fast central jet and low pressure (Venturi effect). Different pressure generates inverted flow when heading towards the blood central

![Figure 6](http://www.elsevier.es)
The Venturi effect and the Bernoulli’s equation. If the flow running through a variable section conduit remains constant when the section diminishes the velocity necessarily increases. According to the Work Energy Theorem the product between velocity (V) and pressure (P) needs to be constant (K). The P difference generated by the high central velocity jet generates a reversed flow (red coils) heading towards the areas with the smallest diameter of all.

In sum the DDU is a safe efficient modality in the study of PVA stenoses and thromboses while providing us with anatomic and hemodynamic information. However prospective studies will be necessary to correlate flow and RI in the afferent arteriole with the dysfunction of the PVA and other variables like the body mass index, sex, age, type of vascular access or peripheral arteriopathy.

**Ethical responsibilities**

**Protection of people and animals.** Authors confirm that for this investigation no experiments with human beings or animals have been carried out.

**Data confidentiality.** Authors confirm that the protocols of their centers have been followed on matters concerning the publishing of data from patients. They also confirm that all patients included in this study have been given enough information and handed over their written informed consent for their participation in this study.
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Right to privacy and informed consent. Authors confirm that they have obtained the written informed prior consent from patients and/or subjects appearing in this article. This document is in the possession of the corresponding author.

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1 Manager of the integrity of the study: TMS.
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3 Study design: TMS, CMH, ESM.
4 Data mining: TMS, ESM.
5 Data analysis and interpretation: TMS, ESM, FMR.
6 Statistical analysis: TMS, CMH, FMR.
7 Reference search: TMS, ESM.
8 Writing: TMS, CMH, ESM, FMR.
9 Manuscript critical review with intellectually relevant contributions: CMH, FMR.
10 Final version approval: TMS, CMH, ESM, FMR.

Conflict of interests

Authors reported no conflicts of interests.

References