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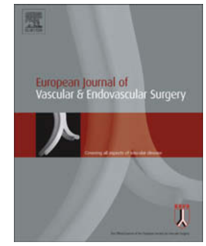

Distensibility of Forearm Veins in Haemodialysis Patients on Duplex Ultrasound Testing Using Three Provocation Methods

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Abstract *Objective:* It is well-known that vasodilatator function is affected in patients with renal failure. We hypothesized impaired venous forearm distensibility in haemodialysis patients. The purpose of this study was to investigate which provocation method generated 'maximal' venous distensibility in the forearm of haemodialysis patients compared to healthy volunteers by using duplex ultrasound.
Design: The study group consisted of haemodialysis patients ($n = 30$) and healthy volunteers ($n = 30$). In each participant ultrasound measurements of the venous diameter were performed by using 3 different provocation methods.
Methods: The applied provocation methods were: 1) hydrostatic pressure, 2) venous congestion and 3) hydrostatic pressure and warmth. Significance of differences in mean diameter changes within the groups was assessed with the paired t-test. Significance of differences in mean diameter changes between the groups was compared by using multivariate regression analysis.
Results: In haemodialysis patients, the increase in mean diameter after the different methods was: 29% after methods 2 versus 1, 23% after methods 3 versus 2 and 59% after methods 3 versus 1. In healthy volunteers, the mean diameter increase was: 27% after methods 2 versus 1, 29% after methods 3 versus 2 and 64% after methods 3 versus 1. The greatest increase in the mean internal venous diameter among the haemodialysis patients and the healthy volunteers was after the provocation method which combined hydrostatic pressure with warmth (mean

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difference: 1 mm, 95% CI: .57, 1.36; $P < .001$ and mean difference: 1.4 mm, 95% CI: .88, 1.78; $P < .001$, respectively). After adjustment for the baseline variables, both groups demonstrated a non-significant mean diameter difference for each of the provocation methods.
Conclusion: Hydrostatic pressure combined with warmth generates the greatest venous distensibility in the lower arm in haemodialysis patients in a sitting position and is not significantly different compared to healthy volunteers. Without the superior provocation method, venous diameters of haemodialysis patients can be assessed as false-negatives yielding that a primary radio cephalic arteriovenous fistula (RCAVF) at wrist level (the first choice) in these patients will be withheld.

Introduction

Vascular access is very important for the quality of life and survival of end-stage renal failure patients requiring haemodialysis. The K-DOQI and European guidelines of the Vascular Access Society recommend a native primary radio cephalic arteriovenous fistula (RCAVF) as the vascular access of first choice for haemodialysis.[1] Duplex ultrasound (DUS) is the recommended imaging modality prior to the surgical construction of a RCAVF. DUS is non-invasive and provides qualitative and quantitative information such as vascular wall irregularities, haemodynamic and anatomical information.[2–5]

The venous system is known for its low-pressure vessels (~15 mmHg) compared to the high-pressure vessels of the arterial system (~120 mmHg). DUS of the venous system in the forearm, however, can sometimes fail due to the low-pressure vessels and relatively small internal diameters.[6] DUS is advised in supine position by the Vascular Access Society.[4] However, the weight of the DUS transducer and the pressure of the investigators hand may compress the low-pressure vessels. These components can make DUS measurements of the venous system of the forearm inaccurate.[7]

Venous distensibility is an important predictor of RCAVF success.[8,9] Several provocation methods are recommended for venous distensibility and consecutive improvement of DUS visualisation.[5,10] DUS can be a very useful preoperative technique in combination with these provocation methods to investigate venous distensibility.[11] Under adequate circumstances and performed by experienced vascular technologists, DUS combined with provocation methods may provide optimal anatomical information and has the potential to visualize small diameter changes.[5,10]

The purpose of this study was to investigate whether different provocation methods that all claim to generate 'maximal' venous distensibility in healthy volunteers, showed the same DUS results in haemodialysis patients.[5] The arterial endothelial vasodilatator function is impaired in patients with renal failure, diabetes, hypertension and heart failure.[12–14] Also defective venous distensibility is demonstrated in patients with renal failure.[15,16] We hypothesized that venous forearm distensibility is impaired in haemodialysis patients, compared to healthy volunteers. In addition, we evaluated the differences in venous distensibility generated by different provocation methods. Furthermore, we evaluated the intra-observer reproducibility of DUS measurements of the internal venous diameters.

Patients and Methods

Study design and patients

From September 2007 until January 2008, we performed a cohort study at the Albert Schweitzer Hospital, Dordrecht, The Netherlands, with a specialized vascular laboratory experienced in the field of haemodialysis patients. The study group consisted of 30 haemodialysis patients and 30 healthy volunteers. Information was recorded about our volunteers' age, sex, height, weight, diabetes mellitus, arterial hypertension, current smoking, non dominant arm, haemodialysis duration and access type.[5,8,17] This research project has been considered and approved by the committee on medical ethics of our institution. Patients and volunteers gave their informed written consent for their inclusion in this study.

Duplex ultrasound examination

Each participant was examined with a 13–5 MHz broadband ultrasound imaging transducer (Aloka, ProSound SSD-5000, SSD-5500 en SSD 3500SV, Aloka, Tokyo, Japan) by an experienced registered vascular diagnostic technologist under the same conditions. In each volunteer two internal venous diameter measurements were measured by DUS using 3 separate provocation methods (6 measurements in each volunteer, noted as measurements 1a,b, 2a,b and 3a,b). The non dominant arm was preferred, which was available in all patients with a haemodialysis vascular access catheter and in all healthy volunteers, although not in patients with an arteriovenous fistula in the arm. All participants were examined in sitting position with the extended arm supported on a table.[5,10,11,18] The height of the table was adapted to the volunteer's arm length, so all participants were examined in the same position. Both the room temperature and the gel temperature were 21–22 °C (69.8–71.6° F). The cephalic vein was identified in the forearm with DUS at a position eight centimetres proximal of the styloid process of the radius. Skin marking was performed prior to DUS measurements with waterproof ink to ensure reproducibility of the scan location. The internal diameter of the cephalic vein was measured twice in the anteroposterior direction in a transverse scan and all measurements were recorded.[19] During DUS measurements, three provocation methods were employed.

Provocation methods

In the first provocation method, hydrostatic pressure was used as a type of physiological vascular provocation. The physiological provocation is caused by the gravitational force in a sitting position, which creates a downward pressure, known as the hydrostatic pressure. This impedes venous return from the lower arm to the heart resulting in dilatation of the veins. External venous compression was avoided by using a moderate quantity of ultrasound gel between the transducer and skin surface.

In the second provocation method, venous congestion was used, generated by a pneumatic cuff inflator. An occlusion cuff around the upper arm (10 cm cuff, 80 mmHg) was used to accomplish 'maximal' distensibility of the cephalic vein in the forearm (Hokanson E20, Hokanson, Bellevue, USA).[10,18] The occlusion time was 2 min and measured with a stopwatch.[5]

In the third provocation method, we combined hydrostatic pressure with a 10 l basin containing warm water in which the forearm was immersed.[5] The water temperature was 43–44 °C (109.4–111.2° F) and measured digitally (Fluke thermocouple 51 K-type, Fluke, Everett, USA). While a stopwatch was running (2 min) the dilatation process was monitored with DUS.[5] When 'maximal' distensibility was reached, measurements were performed keeping the forearm in the warm water. External thermal influences were eliminated by immersion of the arm which works as ultrasound conductor instead of the usual conducting gel. Provocation methods were always performed in this sequence.

Statistical analysis

All baseline characteristics of the participants were expressed as means and standard deviation (SD). Because of the non-normal distributions of the baseline characteristics of the participants, comparisons between the haemodialysis patients and the healthy volunteers were tested with the non-parametric Mann–Whitney *U* test. Dichotomous variables were tested with the Chi-square test. Significance of differences in mean diameter changes after provocation within the two groups was assessed with the paired *t*-test and was evaluated for the three provocation methods separately. Significance of differences in mean diameter changes after provocation between the two groups was assessed with the two-sample *t*-test and was evaluated for the three provocation methods separately. In addition, we used multivariate regression analysis, with variables potentially having significant influence. The variables included were age, sex, height, weight, diabetes mellitus, arterial hypertension, current smoking, non dominant arm, haemodialysis duration and access type. These variables were selected based on literature and clinical judgement.[5,8,17]

Agreement between two provocation methods (methods 1 versus 2, 2 versus 3 and 1 versus 3) was plotted using Bland–Altman graphs enabling an appreciation of the distribution of error.[20] We first performed a bias correction for the values of methods 2 and 3, which was induced by a consistently higher increase in the diameters after provocation methods 2 and 3. In these graphs we were not interested in the difference between the three methods but we would assess whether the new method agrees sufficiently well with the old method. Intra-observer variability was assessed by using a weighted Kappa.[21] In addition, Bland and Altman plots were used to test the agreement of the intra-observer repeatability for each provocation method (measurement 1a versus 1b, 2a versus 2b and 3a versus 3b). Significance was determined at the 95% confidence interval (two-sided, $P < .05$). SPSS 14.0 software for Windows (SPSS Inc., Chicago, Illinois, USA) and STATA 10.0 software for Windows (STATACorp., Texas, USA) were used.

Results

Table 1 shows the baseline characteristics of the two study groups. The variables 'height' and 'weight' were evenly distributed (*P*-values .94 and .85 respectively), whereas age, sex, diabetes mellitus, arterial hypertension, current smoking and non dominant arm were not ($P < .05$) (Table 1). Among the haemodialysis patients, 15 of 30 left arms and 15 of 30 right arms examined. Among the healthy volunteers 27 of 30 (90%) left arms and 3 out of 30 (10%) right arms were examined. Among the haemodialysis patients the mean haemodialysis duration was 40 months (range 2–195;

Table 1 Baseline characteristics of the participants[a]

Characteristic	Dialysis patients ($n = 30$) n (%)	Healthy volunteers ($n = 30$) n (%)	*P*-value
Age (y)	68 (12.7)	49 (17.1)	<0.001
Male gender, %	20 (67)	7 (23)	0.001
Height (m)	1.71 (0.1)	1.71 (0.01)	0.94
Weight (kg)	74 (12.0)	75 (10.6)	0.85
Current smoking, %	8 (27)	2 (7)	0.04
Diabetes mellitus, %	9 (30)	0 (0)	0.001
Arterial hypertension, %	6 (20)	0 (0)	0.01
Left arm, %	15 (50)	27 (90)	0.001

[a] Descriptors are mean (SD), dichotomous values as number and percentage in parentheses.

Table 2 Comparison between three different provocation methods used for the measurement of the internal venous diameter among haemodialysis patients and healthy volunteers

Provocation method	Dialysis patients ($n = 30$) mean diameter difference (95% CI)[a]	*P*-value	Healthy volunteers ($n = 30$) mean diameter difference (95% CI)[a]	*P*-value
1 versus 2 (mm)	−0.5 (−0.85, −0.11)	0.01	−0.6 (−1.14, −0.09)	0.02
2 versus 3 (mm)	−0.5 (−0.88, −0.08)	0.02	−0.7 (−1.19, −0.25)	0.01
1 versus 3 (mm)	−1.0 (−1.36, −0.57)	<0.001	−1.3 (−1.78, −0.88)	<0.001

[a] Negative difference indicates that the last mentioned provocation method has a better outcome. (Provocation method 1 = hydrostatic pressure, provocation method 2 = venous congestion and provocation method 3 = hydrostatic pressure and warmth. CI = confidence interval).

SD 41). The type of vascular access used for haemodialysis among the haemodialysis patients was tunnelled catheters in 67% (20 out of 30) and fistulae in 33% (10 out of 30).

After provocation method 1, internal venous diameters of haemodialysis patients ranged from 0.6 to 4.1 mm. After provocation method 2, from 1 to 4.6 mm and after provocation method 3, from 1.6 to 5.1 mm. After provocation method 1, internal venous diameters of healthy volunteers ranged from 0.7 to 4 mm. After provocation method 2, from 1 to 4.7 mm and after provocation method 3, from 2 to 4.9 mm. Table 2 shows the comparison between three different provocation methods used for the measurement of the internal venous diameter among haemodialysis patients and healthy volunteers.

Haemodialysis patients showed an increase of the mean diameter of 29% after provocation method 2 compared to provocation method 1. After provocation method 3 compared to provocation method 2 the increase was 23%, and compared to provocation method 1 this was 59%. Healthy volunteers showed an increase of the mean diameter of 27% after provocation method 2 compared to provocation method 1. After provocation method 3 compared to provocation method 2 the increase was 29% and compared to provocation method 1 this was 64%. Table 3 shows the comparison between the two study groups of the mean internal venous diameters for each provocation method.

Agreement between two provocation methods is represented in Bland and Altman plots (Fig. 1a–c) (methods 1 versus 2, 2 versus 3 and 1 versus 3). The plots show an acceptable agreement between the different provocation methods.[20] Differences were within the limits of agreement, except for one outlier in the agreement between provocation methods 1 versus 3.

Agreement of the intra-observer repeatability for each provocation method (measurements of provocation methods 1, 2 and 3) was represented in Bland and Altman plots.[20] The differences were within the limits of agreement (the mean difference for all 3 plots was: 0 mm and the SD respectively: 0.8, 0.7 and 0.7). Except for one outlier in the agreement for provocation methods 1 and 3 and two outliers in the agreement for provocation method 2. Weighted Kappa values for the first, second and third provocation methods were: 0.97, 1.00 and 0.93 respectively, indicating an 'almost perfect' strength of agreement.[21]

Discussion

This study assessed whether different provocation methods that generate 'maximal' venous distensibility in healthy volunteers showed the same DUS results in haemodialysis patients. Comparing these groups, the main finding of our study was that venous diameters were statistically significant larger with a combination of hydrostatic pressure and warmth in both haemodialysis patients and healthy volunteers. After adjusting for all baseline variables we found no

Table 3 Comparison between the two study groups of the mean internal venous diameters for each provocation method

Provocation method	Dialysis patients ($n = 30$) mean diameter (95% CI)	Healthy volunteers ($n = 30$) mean diameter (95% CI)	Unadjusted mean difference (95% CI)[a]	Adjusted mean difference (95% CI)[a,b]	Adjusted *P*-value
Method 1 (mm)	1.7 (1.45, 1.95)	2.2 (1.85, 2.55)	−0.5 (−0.95, −0.07)	−0.1 (−1.58, 1.35)	0.87
Method 2 (mm)	2.2 (1.94, 2.46)	2.8 (2.42, 3.17)	−0.6 (−1.11, −0.18)	−0.2 (−1.74, 1.40)	0.83
Method 3 (mm)	2.7 (2.41, 2.99)	3.6 (3.34, 3.86)	−0.9 (−1.28, −0.48)	−1.1 (−2.50, 0.23)	0.10

[a] Negative difference indicates healthy volunteers have a better outcome.
[b] Adjusted for baseline independent variables: age, gender, length, weight, current smoking, diabetes mellitus, hypertension, non dominant arm, haemodialysis duration and access type. (Provocation method 1 = hydrostatic pressure, provocation method 2 = venous congestion and provocation method 3 = hydrostatic pressure and warmth. CI = confidence interval).

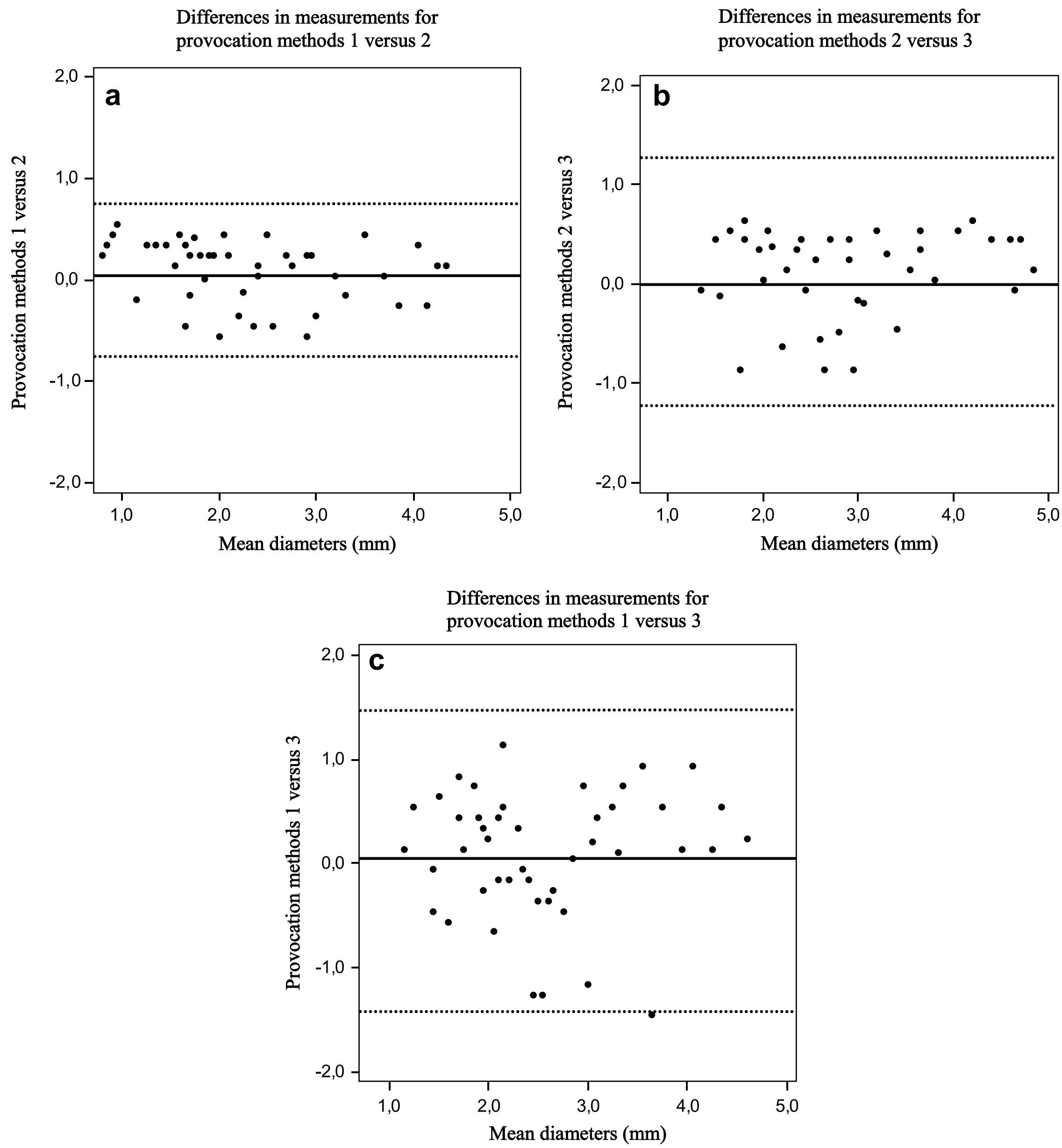

Figure 1 **a** Bland—Altman plot represents the mean of the measurements (*x*-axis) versus the difference between the two values for provocation methods 1 versus 2 (*y*-axis). The solid line shows the mean difference (0.01 mm). The dashed lines $2 \times$ SD (SD = 0.4). **b** Bland—Altman plot represents the mean of the measurements (*x*-axis) versus the difference between the two values for provocation methods 2 versus 3 (*y*-axis). The solid line shows the mean difference (0 mm). The dashed lines $2 \times$ SD (SD = 0.6). **c** Bland—Altman plot represents the mean of the measurements (*x*-axis) versus the difference between the two values for provocation methods 1 versus 3 (*y*-axis). The solid line shows the mean difference (0.01 mm). The dashed lines $2 \times$ SD (SD = 0.7).

statistically significant difference in venous distensibility between haemodialysis patients and healthy volunteers. This suggests that the most effective provocation method (hydrostatic pressure combined with warmth) should be used in haemodialysis patients. The intra-observer reproducibility for all provocation methods was almost perfect.

A previous study showed that the results in healthy volunteers were reproducible.[5] The effect of a provocation method which combines hydrostatic pressure and warmth (without venous congestion) had already been tested in normal volunteers in sitting position. Significantly larger diameters were found in normal arm veins after provocation.[5] The previous study assumed that larger venous diameters would best predict the venous diameter post-operatively caused by arterial pressure.[5] However, no study has been reported in which venous distensibility in haemodialysis patients was investigated using combined warmth and hydrostatic pressure to provoke venodilation.

Venous distensibility of the forearm was studied by Van Der Linden et al. using strain-gauge plethysmography compared to DUS examination.[9] The authors conclude that 'forearm venous distensibility is a predictor of AVF success, whereas DUS derived luminal diameters are not.' The DUS protocol (examination in patients in supine position, without venous congestion) used by these authors was not consistent with the plethysmography protocol (with venous congestion). In our study we investigated all participants in the sitting position using different provocation methods.[5] Plethysmography calculates volume changes in the forearm, without the ability to discriminate between anatomical structures. In addition, although plethysmography is an interesting technique in a scientific setting, few vascular laboratories are equipped to perform this test. DUS provides direct physiological information as well as anatomical information.

Several possible limitations of this study warrant consideration. The first limitation of the present study was the study design, because our reference group was not pair-matched to the case population. This resulted in statistically significant differences of the baseline characteristics between the two study groups. A number of these baseline variables were subsequently used to adjust for potential confounding by performing multivariate regression analysis. The next limitation might be the absence of an inter observer reproducibility test in DUS measurement. Instead we have investigated the intra-observer reproducibility, because this was the only method feasible in our setting.

The present study showed that there were no statistically significant differences in venous distensibility between haemodialysis patients and healthy volunteers following the three provocation methods. In accordance with the guidelines of the American K-DOQI, venous diameters at wrist level has to be at least 2,5 mm.[3] European Vascular Access Society guidelines suggest at least 2.0 mm in supine position.[4] Based on these guidelines, we suggest that the superior provocation method (hydrostatic pressure combined with warmth) should be applied, when small internal diameters are found in sitting haemodialysis patients with the first provocation method (hydrostatic pressure) and the second provocation method (venous congestion). Without the superior provocation method, venous diameters of haemodialysis patients can be assessed as false-negatives yielding that a primary RCAVF at wrist level (the first choice) in these patients will be withheld.

Now we are able to approach the distensibility issue practically in the preoperative DUS examination setting at the vascular laboratory. The present study showed that hydrostatic pressure and warmth increases the venous distensibility and creates the opportunity for more haemodialysis patients to be qualified for a primary RCAVF at wrist level, which is the vascular access of first choice for haemodialysis. We suggest further investigation of preoperative DUS and provocation methods in association with patency. The results of our study may help to develop future research in this field.

Conflict of Interest/Funding

None.

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References

1 Brescia M, Cimino J, Appel K, Hurwich B. Chronic hemodialysis using venipuncture and a surgically created arteriovenous fistula. *New Engl J Med* 1966;**275**:1089–92.

2 National Kidney Foundation-Dialysis Outcomes Quality Initiative. The vascular access workgroup NKF-DOQI clinical practice guidelines for vascular access. *Am J Kidney Dis* 1997;**30** (Suppl. 3):S152–91.

3 National Kidney Foundation. K/DOQI clinical practice guidelines for vascular access. *Am J Kidney Dis* 2000;**37**(Suppl. 1):S137–81.

4 Bakran A, Mickley V, Passlick-Deetjen J. *Management of the renal patient: clinical algorithms on vascular access for haemodialysis*. Lengerich: Pabst Science Publishers; 2003.

5 Van Bemmelen PS, Kelly P, Blebea J. Improvement in the visualization of superficial arm veins being evaluated for access and bypass. *J Vasc Surg* 2005;**42**:957–62.

6 Rumack CM, Wilson SR, Charboneau JW, Johnson JAM. *Diagnostic ultrasound*. 3rd ed. St. Louis Missouri: Elsevier Mosby; 2005.

7 Planken RN, Tordoir JHM, Duijm LEM, van den Bosch HC, van der Sande FM, Kooman JP, et al. Magnetic resonance angiographic assessment of upper extremity vessels prior to vascular access surgery: feasibility and accuracy. *Eur Radiol* 2008;**18**:158–67.

8 Malovrh M. Native arteriovenous fistula: preoperative evaluation. *Am J Kidney Dis* 2002;**39**:1218–25.

9 Van der Linden J, Lameris TW, Van Den Meiracker AH, De Smet AA, Blankestijn PJ, Van Den Dorpel MA. Forearm venous distensibility predicts successful arteriovenous fistula. *Am J Kidney Dis* 2006;**47**(6):1013–9.

10 Korten E, Toonder IM, Schrama YC, Hop WCJ, van der Ham AC, Wittens CHA. Dialysis fistulae patency and preoperative diameter ultrasound measurements. *Eur J Vasc Endovasc Surg* 2007; **33**:467–71.

11 Korten E, Wittens CHA, Diderich PPNM. *Vasculaire toegang voor hemodialyse patiënten — non-invasieve preoperatieve screening op het vaatlaboratorium*. Rotterdam: Saint Franciscus Hospital; 2004.

12 London GM, Marchais SJ, Guerin AP, Metivier F, Adda H. Arterial structure and function in end-stage renal disease. *Nephrol Dial Transplant* 2002;**17**:1713–24.

13 Anderson TJ. Assessment and treatment of endothelial dysfunction in humans. *J Am Coll Cardiol* 1999;**34**(3):631–8.

14 Guérin AP, Pannier B, Marchais SJ, London GM. Arterial structure and function in end-stage renal disease. *Curr Hypertens Rep* 2008;**10**(2):107–11.

15 Kooman JP, Wijnen JA, Draaijer P, van Bortel LM, Gladziwa U, Peltenburg HG, et al. Compliance and reactivity of the peripheral venous system in chronic intermittent hemodialysis. *Kidney Int* 1992;**41**(4):1041–8.

16 Bradley JR, Evans DB, Cowley AJ. Abnormalities of the peripheral circulation in patients with chronic renal failure. *Nephrol Dial Transplant* 1988;**3**(4):412–6.

17 Rooijens PPGM, Tordoir JHM, Stijnen T, Burgmans JPJ, de Smet AAEA, Yo TI. Radiocephalic wrist arteriovenous fistula for hemodialysis: meta-analysis indicates a high primary failure rate. *Eur J Vasc Endovasc Surg* 2004;**18**:583–9.

18 Gardner GP, Cordts PR, Gillespie DL, Lamorte W, Woodson J, Menzoain JO. Can air plethysmography accurately identify upper extremity deep venous thrombosis? *J Vasc Surg* 1993;**18**:808–13.

19 Mohler III ER, Gerhard-Herman M, Jaff MR. *Essentials of vascular laboratory diagnosis*. Oxford: Blackwell Publishing; 2005.

20 Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *The Lancet* 1986;**I**:307–10.

21 Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977;**33**:159–74.