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Comparative Profiling of Arterial Stiffness and Radiocephalic Arteriovenous Fistula Morphology in Diabetic Versus Non-Diabetic Patients on Maintenance Hemodialysis

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ABSTRACT

Background: Diabetes mellitus accelerates cardiovascular deterioration in chronic kidney disease, but it is unclear whether it adds stiffness to the central arteries or affects the peripheral arteriovenous fistula (AVF) of hemodialysis patients.

Objective: To compare central and peripheral pulse wave velocity (cfPWV, faPWV), renal resistive index (RI), and radiocephalic AVF diameter and volume flow between diabetic and non-diabetic hemodialysis patients.

Methods: This analytical cross-sectional study included 120 prevalent hemodialysis patients (22 diabetic, 98 non-diabetic) at Dr. M. Djamil General Hospital in 2025. One blinded sonographer measured the vascular parameters by Doppler ultrasonography. Groups were compared with t-tests and chi-square tests, with 95% confidence intervals and Cohen's d.

Results: Diabetic patients were older (56.4 ± 8.1 vs. 50.6 ± 9.4 years; $p = 0.004$) and had lower diastolic blood pressure (73.27 ± 9.84 vs. 79.72 ± 10.15 mmHg; $p = 0.008$). cfPWV (2.89 ± 0.57 vs. 2.90 ± 0.61 m/s; $p = 0.941$), faPWV (3.34 ± 0.73 vs. 3.15 ± 0.69 m/s; $p = 0.236$), and mean RI (0.825 ± 0.029 vs. 0.818 ± 0.033 ; $p = 0.341$) did not differ. AVF diameter was smaller in diabetic patients (1.74 ± 0.63 vs. 2.36 ± 0.74 mm; $p < 0.001$; Cohen's $d = -0.86$), whereas flow did not differ significantly (3489 ± 1018 vs. 3063 ± 945 mL/min; $p = 0.072$).

Conclusion: Diabetes was associated with a smaller AVF diameter but not with higher central or peripheral stiffness or renal RI. Given the cross-sectional, unadjusted design, adjusted longitudinal studies are needed.

1. Introduction

Chronic kidney disease (CKD) is a growing global health problem. It involves progressive loss of renal parenchymal function, persistent microalbuminuria, and a heavy burden of cardiovascular morbidity and mortality.^{1,2} According to global epidemiological estimates, CKD affects roughly 850 million people worldwide, or 9.1% to 13.4% of adults. It is the twelfth leading cause of death and is projected to become the fifth leading cause of years of life lost by 2040.³⁻⁶ The Kidney Disease: Improving Global Outcomes (KDIGO) guideline defines CKD as abnormal kidney structure or function that lasts more than three months, and it classifies patients by glomerular filtration rate (G1 to G5) and albuminuria (A1 to A3).⁷ In Southeast Asia and other developing regions, rapid urbanization and lifestyle change have fueled an epidemic of type 2 diabetes mellitus and hypertension. Together these two conditions account for 65% to 75% of incident end-stage kidney disease (ESKD) cases that need

maintenance renal replacement therapy.⁸ Nephron loss itself involves chronic activation of pro-fibrotic signaling, transforming growth factor-beta (TGF- β) transactivation, and microvascular rarefaction, which end in destruction of the renal parenchyma.⁹ Environmental nephropathies add to this picture, since chronic kidney disease of unknown etiology (CKDu) shows how toxic, occupational, and hemodynamic insults combine to cause kidney failure in many populations.¹⁰ Cardiovascular disease dominates mortality once ESKD is treated by maintenance hemodialysis, causing more than half of all deaths. The usual modes are fatal arrhythmia, acute coronary syndrome, sudden cardiac death, and refractory heart failure.^{11,12} Traditional Framingham risk factors do not fully explain this excess mortality. It reflects a distinct uremic vascular phenotype with premature vascular senescence, diffuse medial calcinosis, and widespread endothelial dysfunction.¹³

The vascular endothelium keeps the vessel wall in balance. It sets vascular tone, prevents thrombosis, limits leukocyte extravasation, and restrains pathological proliferation of vascular smooth muscle cells (VSMCs).^{14,15} Under healthy conditions, endothelial nitric oxide synthase (eNOS) converts L-arginine stereospecifically into nitric oxide (NO). This continuous NO output preserves conduit artery compliance and microcirculatory perfusion.^{16,17} Advanced uremia changes this. Protein-bound retention solutes (indoxyl sulfate, p-cresyl sulfate, and kynurenine metabolites) accumulate, and so do small water-soluble molecules such as asymmetric dimethylarginine (ADMA). Both groups injure the endothelium.^{18–20} These toxins raise the activity of intracellular nicotinamide adenine dinucleotide phosphate (NADPH) oxidase and disturb mitochondrial electron transport complexes. The result is a large output of reactive oxygen species (ROS), including superoxide anions ($O_2^{\bullet-}$) and hydrogen peroxide (H_2O_2).²¹ Superoxide reacts quickly with endothelial NO and forms peroxynitrite ($ONOO^-$), a cytotoxic reactive nitrogen species. Peroxynitrite oxidizes tetrahydrobiopterin (BH4), the cofactor eNOS needs, and eNOS becomes uncoupled.^{22,23} The uncoupled enzyme makes superoxide in place of NO. This is a vicious circle. Bioavailable NO falls and nuclear factor-kappa B (NF- κ B) is activated. VSMCs switch to a synthetic, osteogenic phenotype, and that switch drives medial calcinosis and stiffening of the arterial wall.²⁴ Arterial stiffness is the loss of elastic recoil in the large conduit arteries, above all the aorta. It is the main hemodynamic result of uremic vascular disease.^{25,26} In a healthy person, the elastic thoracic aorta acts as a hydraulic capacitor, known as the Windkessel effect. It expands during left ventricular ejection and stores part of the stroke volume, then recoils in diastole, which keeps forward flow continuous and supports coronary perfusion.²⁶ Pulse wave velocity (PWV) follows from the Moens-Korteweg and Bramwell-Hill equations. It varies inversely with vessel distensibility and directly with the elastic modulus and wall thickness of the arterial segment.^{25,26} Carotid-femoral PWV (cfPWV) is the accepted clinical standard for non-invasive measurement of central aortic stiffness. Magnetic resonance imaging and Doppler ultrasonography give reference assessments of arterial distensibility.²⁷ A meta-analysis of longitudinal studies showed that each 1 m/s rise in aortic PWV corresponds to an age-, sex-, and risk factor-adjusted increase of 14% in total cardiovascular events and 15% in cardiovascular and all-cause mortality, with larger effects in high-risk groups such as renal disease.²⁸ The effect is stronger in CKD. Medial calcinosis, fragmentation of elastin fibers, and collagen cross-linking speed up the pulse wave, and a faster pulse wave is a strong predictor of residual renal function loss and adverse cardiovascular outcomes.²⁹

Hemodialysis itself adds repeated hemodynamic stress to the vessels.³⁰ Fluid accumulates between sessions and creates a chronic volume load that stretches the arterial wall, raises wall tension, and drives vascular remodeling.³¹ Rapid fluid removal during ultrafiltration often causes intradialytic hypotension and brief subclinical myocardial and mesenteric ischemia. These events lead to sympathetic activation, repeated endothelial stress, and higher arterial stiffness.³⁰ Diabetes adds a second insult. When it coexists with end-stage uremia, a further metabolic burden is placed on the vasculature.³² Chronic hyperglycemia promotes non-enzymatic glycation of basic amino groups on long-lived vascular proteins. Advanced glycation end-products (AGEs) then form irreversibly and accumulate in tissue, for example N ϵ -(carboxymethyl)lysine (CML) and pentosidine.³³ Circulating and tissue-bound AGEs bind the receptor for advanced glycation end-products (RAGE) on endothelial cells, VSMCs, and infiltrating monocytes. This starts a signaling cascade through p38 mitogen-activated protein kinase (p38 MAPK) and NF- κ B.³³ RAGE ligation sustains transcription of pro-inflammatory cytokines, chemokines, and adhesion molecules. Vascular calcification accelerates. Adventitial fibrosis and microangiopathy of the vasa vasorum follow.^{32,34}

Systemic stiffness is only one part of vascular health in hemodialysis, and the integrity of the vascular access matters just as much, because it is the patient's lifeline.^{35,36} Brescia and Cimino introduced the autogenous radiocephalic arteriovenous fistula (AVF).³⁷ It remains the preferred access because its long-term patency is better and its infection rate lower than those of synthetic grafts or central venous catheters.³⁶ Anastomosing the radial artery to the cephalic vein, however, exposes a thin-walled, low-pressure vein to arterial pressure. Blood flow rises 10- to 20-fold at once.^{35,38} The fistula must then remodel outward to mature. Laminar shear stress prompts the endothelium to release NO, prostacyclin, and matrix metalloproteinases (MMP-2 and MMP-9). The feeding artery and draining vein then widen to the caliber needed for routine twin-needle cannulation, typically ≥ 5 -6 mm.^{35,36} Many fistulas do not reach this caliber. Up to 40% to 60% of radiocephalic AVFs fail to mature or develop early stenosis and thrombosis.^{35,39} Diabetic patients show worse primary patency in most studies, although reports on fistula maturation are heterogeneous.^{40,41}

Pre-existing vascular disease in diabetic patients is strongly linked to access failure.^{40–42} Diabetic vessels often show medial calcification, reduced flow-mediated vasodilation, and advanced adventitial fibrosis. These changes restrict how far the cephalic vein and radial artery can expand outward.^{35,42} High shear stress and disturbed turbulent flow at the anastomotic curve then favor inward neointimal hyperplasia. VSMCs transdifferentiate into migratory osteochondrogenic myofibroblasts, platelet-derived growth factor (PDGF)

is secreted, and adventitial fibroblasts are activated.^{35,38} The inward lesion narrows the lumen and creates a hemodynamic stenosis. Velocity through the narrowed aperture rises, shear-induced platelet activation increases, and access thrombosis follows.³⁸ Much has been written about how uremic toxins and glycemic toxicity converge. Less is known about how macrovascular remodeling and access-specific remodeling diverge in prevalent hemodialysis patients.^{13,35} It is uncertain whether diabetes adds central arterial stiffness (higher cfPWV) or renal parenchymal resistance (higher RI) in a population already under heavy calcific pressure from uremia-related chronic kidney disease-mineral and bone disorder (CKD-MBD). It is equally uncertain whether its harm is confined to the surgically manipulated vessels of the peripheral access.^{13,42,43} Earlier studies disagree: some small series reported higher PWV in diabetic dialysis patients, whereas larger hemodialysis surveys found similar stiffness in both glycemic groups, which suggests that advanced uremic calcification may reach a physiological ceiling.^{29,44} Regional data are scarce. From Southeast Asian hemodialysis units, we found no study that compared pulse wave velocity, renal resistive index, and ultrasound-derived AVF dimensions within one cohort.

Aim of the study

To address these gaps, this study compares central arterial stiffness (cfPWV), peripheral femoral-ankle arterial stiffness (faPWV), renal resistive index (RI), and radiocephalic AVF dimensions (lumen diameter and volume flow rate). The comparison is between diabetic and non-diabetic ESKD patients on chronic maintenance hemodialysis at Dr. M. Djamil General Hospital, Padang. We hypothesized that the uremic milieu would impose a similar ceiling effect on central macrovascular elasticity in both glycemic groups. We further hypothesized that diabetes mellitus would reduce the caliber of the peripheral arteriovenous access. If so, systemic arterial stiffness and local access remodeling would dissociate in a clinically relevant way. Clarifying these differences should refine preoperative vascular mapping, improve access surveillance, and guide treatment in this high-risk population.

2. Methods

Study design and setting

This was an analytical, cross-sectional, single-center observational study. It took place in the Hemodialysis Unit of the Department of Internal Medicine, Dr. M. Djamil General Hospital / Faculty of Medicine, Universitas Andalas, Padang, West Sumatra, Indonesia. The protocol followed the ethical principles of the Declaration of Helsinki (revised Fortaleza, 2013). The Ethics Committee CMHC Research Center Indonesia reviewed it and granted ethical approval (Reference number 2024/297). Each patient gave written

informed consent after receiving verbal and written information on the non-invasive nature, objectives, and procedures of the vascular examinations. Patient anonymity and data confidentiality were maintained throughout data collection and analysis. Personal identifiers were replaced with alphanumeric codes. This report follows the STROBE statement for cross-sectional studies.

Study population and selection criteria

We enrolled 120 consecutive prevalent adult ESKD patients on chronic maintenance hemodialysis between January 2025 and December 2025. Patients were stratified into two cohorts by the documented primary cause of renal failure and by glycemic status. The first was CKD with diabetes mellitus (diabetic group, $n = 22$). It was defined by American Diabetes Association (ADA) criteria, with confirmed diabetic nephropathy as the primary cause of renal failure or longstanding documented type 2 diabetes mellitus before dialysis began. The second was CKD without diabetes mellitus (non-diabetic group, $n = 98$). ESKD in this group resulted from chronic glomerulonephritis, primary hypertensive nephrosclerosis, obstructive uropathy, or other non-diabetic causes, and there was no clinical or biochemical history of diabetes mellitus.⁷ Inclusion criteria were as follows: age ≥ 18 years, either sex; maintenance hemodialysis twice or thrice weekly for at least 3 consecutive months; a functioning autogenous radiocephalic arteriovenous fistula in the upper extremity; and ability to undergo a complete non-invasive vascular Doppler examination. Exclusion criteria were as follows: hemodynamic instability needing continuous inotropic support during the evaluation; active severe systemic sepsis or overt localized vascular graft infection; deep venous thrombosis of an upper or lower limb, or severe peripheral arterial occlusive disease that precluded limb pulse recording; active atrial fibrillation or malignant arrhythmia that interfered with pulse transit-time acquisition; prior bilateral limb amputation; and refusal of informed consent.

Arterial stiffness assessment (pulse wave velocity)

Central and peripheral arterial stiffness were measured with high-resolution Doppler ultrasonography (Mindray DC-70 / GE Logiq S8). High-frequency linear array transducers (7.5-10.0 MHz) and convex transducers (3.5-5.0 MHz) were used. One certified vascular ultrasonographer performed all examinations and was blinded to the clinical and biochemical subgroups.^{25,27} Patients lay supine after at least 15 minutes of quiet rest in a temperature-controlled room (22-24°C). Examinations took place on a mid-week non-dialysis day or just before the scheduled dialysis session. This limited the confounding effect of acute post-dialysis ultrafiltration and intravascular volume depletion.^{30,31} Carotid-femoral pulse wave velocity (cfPWV) reflects central aortic stiffness. We obtained simultaneous or electrocardiogram (ECG)-gated pulse

transit waveforms at the right common carotid artery and the right common femoral artery.^{25,26} An inelastic measuring tape gave the surface distance between the two sites. The distance was calculated by the standard subtraction method, that is, suprasternal notch-to-femoral distance minus suprasternal notch-to-carotid distance.^{25,27} Pulse transit time (ΔT) was the delay between the foot of the carotid systolic upstroke and the foot of the femoral pulse wave. We averaged it over 5 to 10 consecutive cardiac cycles.²⁵ cFPWV was calculated as Distance / ΔT and expressed in m/s.²⁵ Femoral-ankle pulse wave velocity (faPWV) reflects muscular arterial stiffness of the lower limb. It was derived in the same way, from the transit time and surface distance between the common femoral artery and the posterior tibial or dorsalis pedis artery at the ankle.^{26,27}

Renal resistive index protocol

Microvascular resistance of the renal parenchyma was assessed in the native kidneys with B-mode and pulsed-wave spectral Doppler ultrasonography, using a 3.5 MHz convex probe.^{45,46} Color Doppler mapping located the intrarenal vessels. The sample volume (2-3 mm gate) was placed in an interlobar or arcuate artery at the corticomedullary junction, with an insonation angle below 60°. Peak systolic velocity (PSV) and end-diastolic velocity (EDV) were recorded from at least three stable, uniform spectral envelopes in each of the right and left kidneys. The Pourcelot resistive index was calculated as $RI = (PSV - EDV) / PSV$.⁴⁵ Right and left kidney RI were measured separately. The mean renal resistive index was the arithmetic average of the two.

Vascular access ultrasonography (AVF caliber and volume flow)

Morphology and hemodynamics of the autogenous radiocephalic arteriovenous fistula were evaluated with an established vascular access ultrasound protocol that follows KDOQI guidelines.^{36,47} The fistula was scanned in longitudinal and transverse planes. The scan ran from the radial artery inflow through the side-to-side or end-to-side anastomosis and along the draining cephalic vein.³⁶ Internal lumen diameter (mm) was measured on transverse B-mode views. The measurement site was a straight, non-tortuous segment of the cephalic vein about 4 to 5 cm proximal to the arteriovenous anastomosis. Focal aneurysmal dilatations, sharp bifurcations, and cannulation puncture sites were avoided.⁴⁷ Vascular access blood flow volume (Flow Rate Volume, mL/min) was obtained by spectral Doppler with angle correction (<60°), and the sample gate covered the whole vessel lumen. The ultrasound software calculated volume flow as Flow Rate = Time-Averaged Mean Velocity (TAV, cm/s) $\times$ Cross-Sectional Area ($\pi \times [d/2]^2$, cm²) $\times$ 60 (s/min), averaged over three cardiac cycles.^{12,47}

Blood pressure and anthropometric measurements

Brachial blood pressure was measured on the non-access arm with a calibrated, validated oscillometric sphygmomanometer (Omron HEM-907, Kyoto, Japan) and a cuff of appropriate size, after 15 minutes of quiet rest. Three readings were taken at 2-minute intervals. Their mean gave systolic blood pressure (SBP, mmHg) and diastolic blood pressure (DBP, mmHg). Systemic pulse pressure (PP, mmHg) was the arithmetic difference between SBP and DBP. Body weight and height were measured on calibrated medical scales to derive body mass index (BMI, kg/m²). Dialysis vintage was the time in months from the first maintenance hemodialysis session to the date of the vascular evaluation.

Statistical analysis

Distributional normality of continuous variables was assessed with the Kolmogorov-Smirnov and Shapiro-Wilk tests and by visual inspection of histograms. Normally distributed variables are given as mean $\pm$ standard deviation (SD). The groups (diabetic vs. non-diabetic) were compared with the two-tailed independent Student's t-test. Mean differences are reported with exact 95% confidence intervals (95% CI) and Cohen's d as the standardized effect size. Categorical variables, such as sex distribution and underlying diagnostic category, are shown as absolute frequencies (n) and percentages (%). They were compared with Pearson's chi-square (χ^2) test. All hypotheses were tested at a two-sided α of 0.05, so $p < 0.05$ denoted statistical significance. About 12 comparisons were made without correction for multiple testing, and p values should be read accordingly. We performed the computations in SPSS version 26.0 (IBM Corp., Armonk, NY, USA) and checked them with the Python libraries NumPy v1.24 and SciPy v1.10.

3. Results

Baseline characteristics

Of the 120 ESKD patients on chronic maintenance hemodialysis, 22 (18.33%) had diabetes mellitus (diabetic group) and 98 (81.67%) had non-diabetic causes of kidney failure (non-diabetic group). The mean age of the whole cohort was 51.7 ± 9.3 years (range: 24 to 72 years). Table 1 and Figure 1A show that the diabetic patients were older than the non-diabetic patients (56.4 ± 8.1 vs. 50.6 ± 9.4 years; mean difference: +5.80 years; 95% CI: 1.86 to 9.74; $t = 2.94$; $p = 0.004$). The cohort had 64 males (53.33%) and 56 females (46.67%), as shown in Table 1 and Figure 1B. Sex distribution differed between the glycemic subgroups. The diabetic group was mostly female (16 females [72.73%] vs. 6 males [27.27%]). The non-diabetic group was mostly male (58 males [59.18%] vs. 40 females [40.82%]; $\chi^2 = 7.35$, $df = 1$, $p = 0.007$). Dialysis vintage was similar in the two cohorts (34.2 ± 18.5 months in diabetic vs. 38.6 ± 22.1 months in non-

diabetic; mean difference: -4.40 months; 95% CI: -14.32 to 5.52; $t = -0.88$; $p = 0.382$; Table 1).

Table 1. Baseline demographic and clinical characteristics of the hemodialysis cohort

Characteristic	Diabetic (n = 22)	Non-diabetic (n = 98)	Total cohort (n = 120)	p value
Age (years), mean $\pm$ SD	56.4 $\pm$ 8.1	50.6 $\pm$ 9.4	51.7 $\pm$ 9.3	0.004*
Female sex, n (%)	16 (72.7)	40 (40.8)	56 (46.7)	0.007†
Dialysis vintage (months), mean $\pm$ SD	34.2 $\pm$ 18.5	38.6 $\pm$ 22.1	37.8 $\pm$ 21.5	0.382

*Independent t-test. †Pearson chi-square test ($\chi^2 = 7.35$, $df = 1$). SD, standard deviation. Male sex: 6 (27.3%) diabetic, 58 (59.2%) non-diabetic, 64 (53.3%) total.

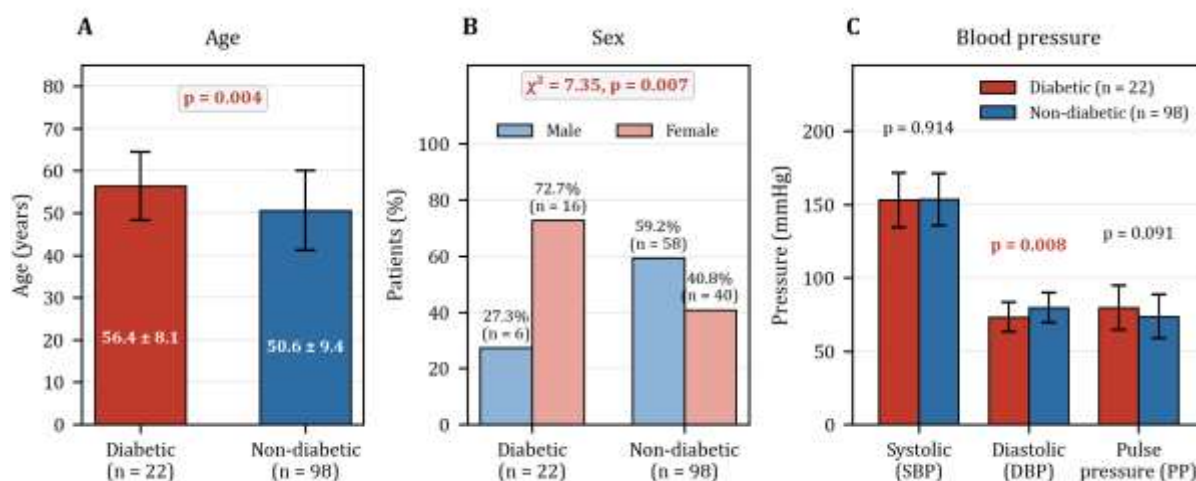


Figure 1. Demographic and systemic resting hemodynamic profile of maintenance hemodialysis patients. (A) Chronological age distribution demonstrating significantly older age in the diabetic cohort ($p = 0.004$). (B) Sex proportions indicating significant female preponderance among diabetic dialysis patients ($\chi^2 = 7.35$, $p = 0.007$). (C) Comparative systemic blood pressure showing equivalent systolic pressure alongside significantly depressed diastolic pressure ($p = 0.008$) and a non-significant difference in pulse pressure ($p = 0.091$). Bars are means and error bars are standard deviations. Values of $p < 0.05$ are shown in red.

Systemic hemodynamics

Resting arterial blood pressure in the two groups is summarized in Table 2 and shown in Figure 1C. Systolic blood pressure (SBP) was almost the same in diabetic and non-diabetic patients (152.91 ± 18.42 mmHg vs. 153.36 ± 17.85 mmHg; mean difference: -0.45 mmHg; 95% CI: -8.65 to 7.75; $t = -0.108$; $p = 0.914$; Table 2, Figure 1C). Mean resting SBP exceeded 150 mmHg in both groups. Diastolic blood pressure (DBP) differed. It was lower in the diabetic cohort than in the non-

diabetic cohort (73.27 ± 9.84 mmHg vs. 79.72 ± 10.15 mmHg; mean difference: -6.45 mmHg; 95% CI: -11.18 to -1.72; $t = -2.71$; $p = 0.008$; Table 2, Figure 1C). Systemic pulse pressure (PP = SBP - DBP) therefore tended to be higher in diabetic patients (79.64 ± 15.20 mmHg vs. 73.64 ± 14.80 mmHg; mean difference: +6.00 mmHg; 95% CI: -0.98 to 12.98; $t = 1.70$; $p = 0.091$; Table 2, Figure 1C). This difference was not statistically significant.

Table 2. Resting systemic hemodynamic profile by diabetes status

Parameter	Diabetic (n = 22)	Non-diabetic (n = 98)	Total cohort (n = 120)	p value
Systolic blood pressure (mmHg)	152.91 $\pm$ 18.42	153.36 $\pm$ 17.85	153.28 $\pm$ 17.96	0.914
Diastolic blood pressure (mmHg)	73.27 $\pm$ 9.84	79.72 $\pm$ 10.15	78.54 $\pm$ 10.35	0.008*
Pulse pressure (mmHg)	79.64 $\pm$ 15.20	73.64 $\pm$ 14.80	74.74 $\pm$ 15.02	0.091

*Independent t-test. Values are mean $\pm$ SD.

Arterial stiffness

Carotid-femoral pulse wave velocity (cfPWV), the standard measure of central aortic stiffness, was very similar in the two cohorts (Table 3, Figure 2A). The mean cfPWV was 2.89 ± 0.57 m/s in diabetic hemodialysis patients and 2.90 ± 0.61 m/s in non-diabetic patients (mean difference: -0.01 m/s; 95% CI: -0.28 to 0.26; $t = -0.074$; $p = 0.941$; Table 3, Figure 2A).

Peripheral arterial stiffness, measured as femoral-ankle pulse wave velocity (faPWV), did not differ significantly either (Table 3, Figure 2B). Values were 3.34 ± 0.73 m/s in diabetic and 3.15 ± 0.69 m/s in non-diabetic (mean difference: +0.19 m/s; 95% CI: -0.13 to 0.51; $t = 1.19$; $p = 0.236$). In the combined cohort of 120 patients, overall cfPWV was 2.90 ± 0.60 m/s and faPWV was 3.18 ± 0.70 m/s (Table 3).

Table 3. Central and peripheral pulse wave velocity in maintenance hemodialysis

Metric	Diabetic (n = 22)	Non-diabetic (n = 98)	Total cohort (n = 120)	p value
cfPWV (m/s), mean $\pm$ SD	2.89 $\pm$ 0.57	2.90 $\pm$ 0.61	2.90 $\pm$ 0.60	0.941
faPWV (m/s), mean $\pm$ SD	3.34 $\pm$ 0.73	3.15 $\pm$ 0.69	3.18 $\pm$ 0.70	0.236

Independent t-test; no comparison reached $p < 0.05$. cfPWV, carotid-femoral pulse wave velocity (aortic stiffness); faPWV, femoral-ankle pulse wave velocity (peripheral arterial stiffness); SD, standard deviation.

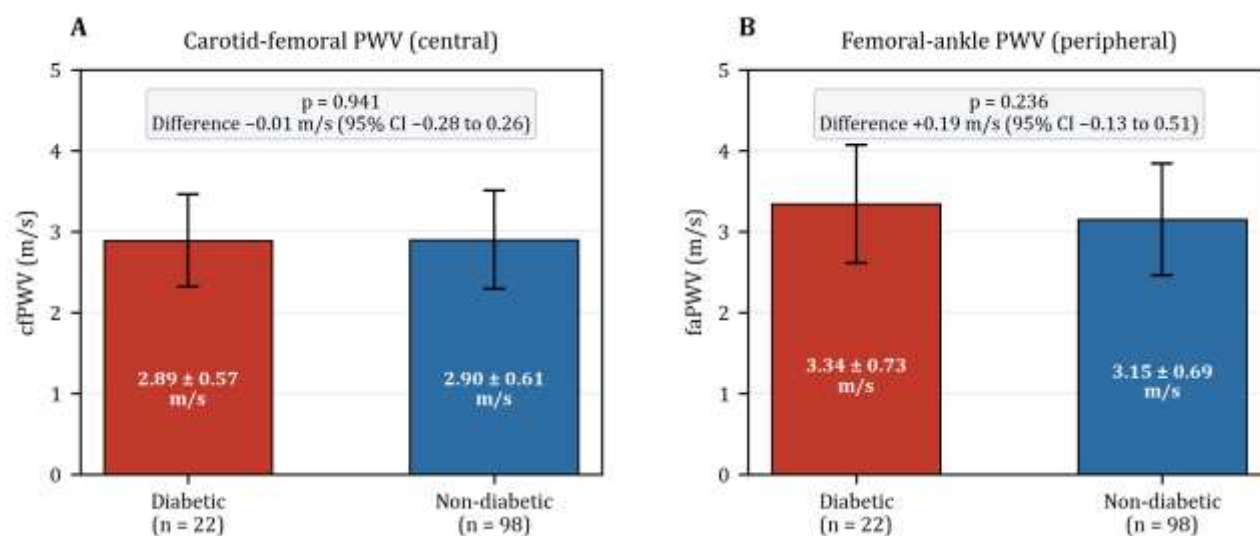


Figure 2. Comparison of central and peripheral pulse wave velocity across glycemic cohorts. (A) Central aortic cfPWV shows no difference between diabetic and non-diabetic cohorts ($p = 0.941$). (B) Peripheral muscular faPWV shows no statistically significant difference ($p = 0.236$). Bars are means and error bars are standard deviations.

Renal resistive index

Spectral Doppler of the native intrarenal arterial microcirculation showed raised resistive index in the entire cohort (Table 4, Figure 3). In the right kidney, mean RI was 0.830 ± 0.037 in diabetic patients and 0.822 ± 0.039 in non-diabetic patients (mean difference: +0.008; 95% CI: -0.010 to 0.026; $t = 0.89$; $p = 0.377$; Table 4, Figure 3). In the left kidney it was 0.820 ± 0.045 in diabetic patients and 0.815 ± 0.056 in non-diabetic patients (mean difference: +0.005; 95%

CI: -0.020 to 0.030; $t = 0.49$; $p = 0.627$; Table 4, Figure 3). The bilateral mean renal RI was 0.825 ± 0.029 in the diabetic group and 0.818 ± 0.033 in the non-diabetic group (mean difference: +0.007; 95% CI: -0.008 to 0.022; $t = 0.96$; $p = 0.341$; Table 4, Figure 3). All recorded RI values were well above the pathological threshold of 0.70. This reflects advanced parenchymal nephrosclerosis and microvascular obliteration, which are common in end-stage kidneys.

Table 4. Native renal resistive index in end-stage kidney disease

Parameter	Diabetic (n = 22)	Non-diabetic (n = 98)	Total cohort (n = 120)	p value
Right kidney RI, mean $\pm$ SD	0.830 $\pm$ 0.037	0.822 $\pm$ 0.039	0.823 $\pm$ 0.039‡	0.377
Left kidney RI, mean $\pm$ SD	0.820 $\pm$ 0.045	0.815 $\pm$ 0.056	0.816 $\pm$ 0.054‡	0.627
Mean bilateral RI, mean $\pm$ SD	0.825 $\pm$ 0.029	0.818 $\pm$ 0.033	0.819 $\pm$ 0.032‡	0.341

Independent t-test; no comparison reached $p < 0.05$. RI, resistive index (reference < 0.70); SD, standard deviation. ‡Computed from the group means and SDs.

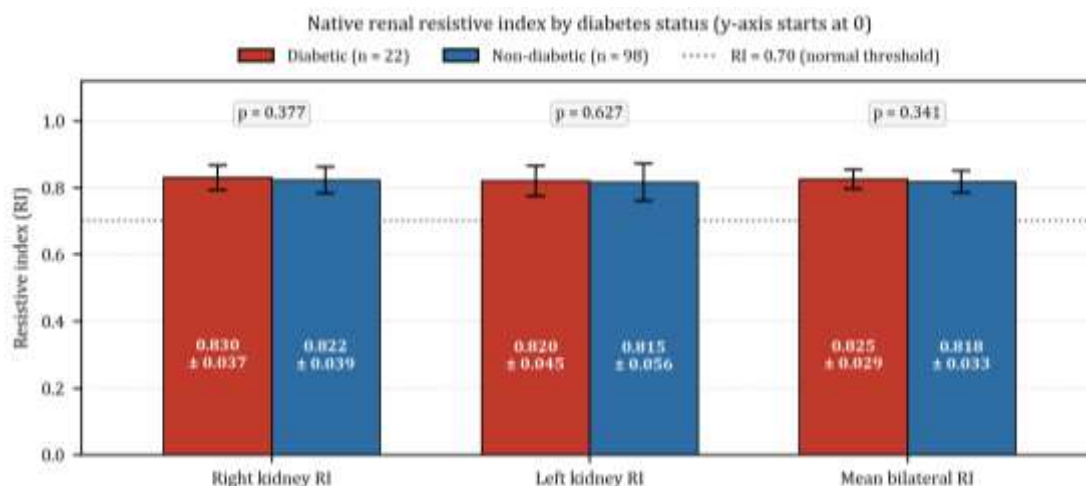


Figure 3. Renal parenchymal resistive index profiles across glycemic subgroups. Both diabetic and non-diabetic cohorts show high microvascular resistance, above the threshold of 0.70, without significant difference across right, left, or mean RI measurements. Bars are means and error bars are standard deviations.

Vascular access caliber and flow volume

Radiocephalic fistula morphology differed from the other parameters. High-resolution ultrasound showed a clear disparity between the groups (Table 5, Figure 4A). The internal lumen diameter of the radiocephalic AVF was smaller in diabetic patients than in non-diabetic patients (1.74 ± 0.63 mm vs. 2.36 ± 0.74 mm; mean difference: -0.62 mm; 95% CI: -0.96 to -0.28 ; $t = -3.65$; $p < 0.001$; Table 5, Figure 4A). The effect size for this difference in caliber was large (Cohen's $d = -0.86$).

It corresponds to a mean luminal diameter reduction of 26.3% in diabetic access vessels. Vascular access blood flow rate volume (Flow Rate Volume) was numerically higher in diabetic patients (3489 ± 1018 mL/min) than in non-diabetic patients (3063 ± 945 mL/min; mean difference: $+426$ mL/min; 95% CI: -39 to 891 ; $t = 1.82$; $p = 0.072$; Table 5, Figure 4B). The difference was not statistically significant, so no conclusion about compensatory flow can be drawn.

Table 5. Morphology and hemodynamics of radiocephalic arteriovenous fistulas

Endpoint	Diabetic (n = 22)	Non-diabetic (n = 98)	Total cohort (n = 120)	Mean difference (95% CI)	p value
AVF lumen diameter (mm)	1.74 ± 0.63	2.36 ± 0.74	2.25 ± 0.76 ‡	-0.62 (-0.96 to -0.28)	$<0.001^*$
Volume flow rate (mL/min)	3489 ± 1018	3063 ± 945	3141 ± 969 ‡	$+426$ (-39 to $+891$)	0.072

*Independent t-test (Cohen's $d = -0.86$). AVF, arteriovenous fistula; CI, confidence interval; SD, standard deviation. ‡Computed from the group means and SDs.

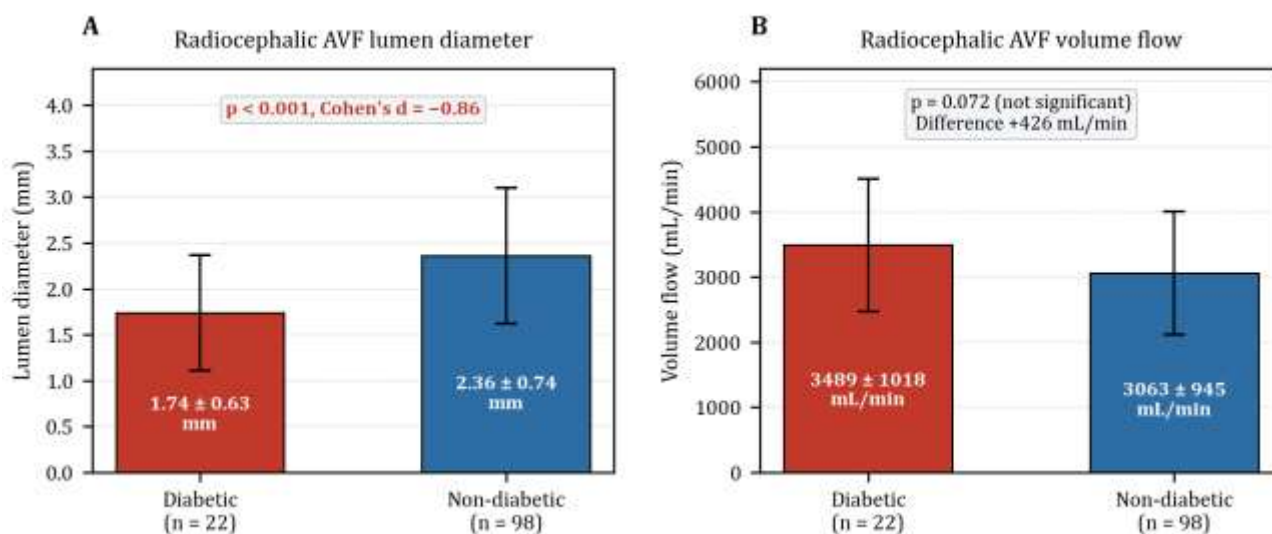


Figure 4. Comparative evaluation of radiocephalic vascular access endpoints. (A) radiocephalic AVF lumen diameter, smaller in diabetic patients ($p < 0.001$, Cohen's $d = -0.86$). (B) Access blood flow rate volume, not significantly different ($p = 0.072$). Bars are means and error bars are standard deviations. Values of $p < 0.05$ are shown in red.

Summary of vascular findings

Taken together, the comparative vascular parameters show a clear pattern. No significant difference between

diabetic and non-diabetic hemodialysis patients was found in systemic aortic stiffness (cfPWV, $p = 0.941$; Table 3), peripheral arterial stiffness (faPWV, $p = 0.236$;

Table 3), or renal parenchymal resistive index (mean RI, $p = 0.341$; Table 4). They differed in radiocephalic fistula caliber. Diabetes mellitus was associated with a narrower lumen of the radiocephalic arteriovenous fistula ($p < 0.001$; Table 5). These cross-sectional findings suggest that, in ESKD, diabetes is associated with a smaller fistula caliber but not with higher central stiffness.

4. Discussion

Principal findings

This observational study shows a clear vascular dissociation in prevalent maintenance hemodialysis patients: macrovascular conduit elasticity (cfPWV, faPWV) and renal parenchymal microvascular resistance (RI) did not differ significantly between the glycemic cohorts, whereas diabetes mellitus was associated with a smaller caliber of the autogenous radiocephalic arteriovenous fistula.^{13,43} Diabetic

patients had a 26.3% smaller radiocephalic AVF lumen than non-diabetic patients (1.74 ± 0.63 mm vs. 2.36 ± 0.74 mm, $p < 0.001$), with a large effect size (Cohen's $d = -0.86$).^{40,43} Carotid-femoral pulse wave velocity, the established standard for central aortic stiffness, was similar in the two groups (2.89 ± 0.57 vs. 2.90 ± 0.61 m/s, $p = 0.941$). So was peripheral muscular arterial stiffness (faPWV: 3.34 ± 0.73 vs. 3.15 ± 0.69 m/s, $p = 0.236$).^{25,28} Renal resistive index was also high. It was uniform in all patients (mean RI: 0.825 vs. 0.818 , $p = 0.341$), far above the physiological threshold of 0.70 .⁴⁵ These observations are compatible with a 'ceiling effect' in uremic macrovascular stiffness, although vascular calcification was not measured here. They also suggest that diabetic vasculopathy in ESKD may act mainly on the peripheral access and not through added central arterial stiffening. Figure 5 summarizes this view.

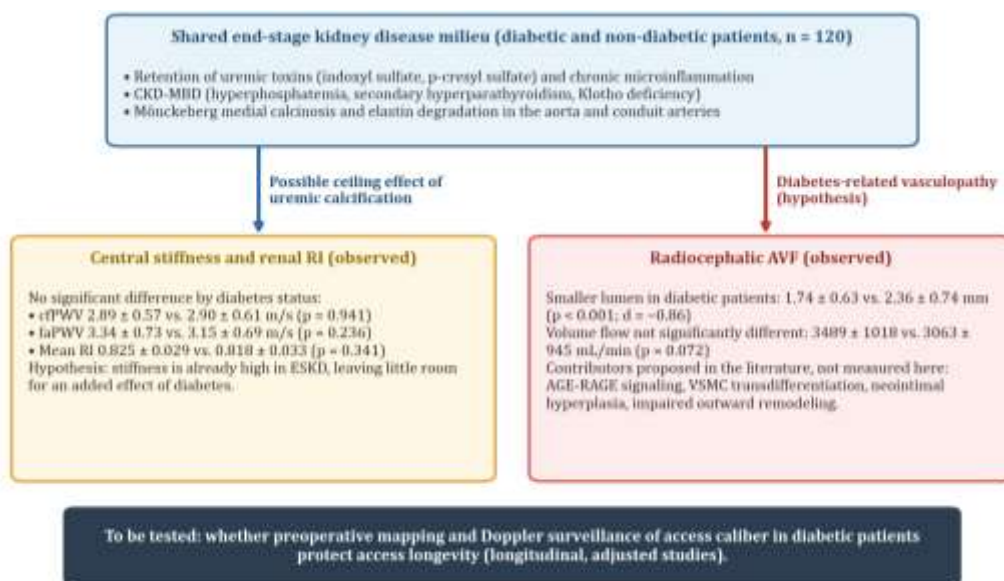


Figure 5. Hypothesized conceptual model illustrating the divergence between macrovascular conduit stiffness and radiocephalic arteriovenous access remodeling in chronic hemodialysis. The shared uremic milieu (hyperphosphatemia, toxic uremic retention, chronic microinflammation) is hypothesized to limit further central aortic stiffening (a possible cfPWV ceiling), whereas diabetic-specific vasculopathy (AGE-RAGE axis, VSMC transdifferentiation, neointimal hyperplasia) may impair outward remodeling of the peripheral access and reduce fistula caliber. None of these mechanisms was measured in this study.

A possible ceiling effect in uremic conduit arteries

Outside the renal population, a large body of clinical and epidemiological work shows that diabetes mellitus accelerates vascular aging and impairs flow-mediated vasodilation. It also raises cfPWV, through hyperglycemia-mediated collagen cross-linking and vascular inflammation.^{32,34} In our hemodialysis patients, however, diabetes had no detectable added effect on aortic or peripheral pulse wave velocity.^{28,29} The pro-calcific, osteochondrogenic milieu of end-stage kidney disease may explain the discordance.^{13,48} In chronic renal failure, disordered mineral-bone metabolism (CKD-MBD) sets off a systemic calcification cascade.^{13,48,49} Hyperphosphatemia, raised circulating fibroblast growth factor-23 (FGF-23), secondary hyperparathyroidism, and deficiency of the anti-aging

hormone soluble Klotho act together to push VSMCs toward osteogenic transdifferentiation.^{13,49} Endogenous mineralization inhibitors, specifically matrix Gla protein (MGP) and fetuin-A, are downregulated, so hydroxyapatite crystals deposit unchecked in the medial layer of elastic and muscular arteries (Mönckeberg medial calcinosis).^{24,48} Protein-bound uremic toxins (indoxyl sulfate and p-cresyl sulfate) are retained as well. They fragment elastin fibers, cross-link collagen, and remodel the vessel wall.^{18,19,21} By the time patients need maintenance hemodialysis, this uremia-driven medial stiffening may have reached a high level, a possible ceiling effect that this study did not test.^{13,44} The added metabolic and glycation insults of diabetes would then be unable to raise conduit stiffness measurably. That would explain

why cFPWV and faPWV did not differ across glycemic categories.

Possible mechanisms linking diabetes to a smaller fistula caliber

The calcified central aorta may be saturated and static. A surgically created arteriovenous fistula is the opposite: a dynamic, actively remodeling system that must adapt greatly before it is clinically mature.^{35,38} Anastomosing the radial artery to the cephalic vein suddenly exposes a low-pressure, thin-walled vein to high arterial pressure and pulsatile shear stress.^{35,38} In a healthy vessel, this stimulus activates endothelial nitric oxide synthase (eNOS), prostacyclin production, and local upregulation of matrix metalloproteinases (MMP-2 and MMP-9). These enzymes degrade the rigid extracellular basement membrane and allow outward eutrophic remodeling. Both the feeding artery and the draining vein dilate progressively, to calibers ≥ 5 -6 mm.^{35,36} In diabetic nephropathy, this program is deranged.^{40,41} Chronic hyperglycemia and tissue accumulation of advanced glycation end-products (AGEs) ligate RAGE on endothelial and smooth muscle cells. NF- κ B is then transactivated continuously, and eNOS is uncoupled through protein kinase C (PKC) activation and reactive oxygen species.^{32,33,50} Endothelial cells in diabetic vessels no longer respond to shear stress and release too little vasodilatory NO.^{16,33} Diabetic microangiopathy of the adventitial vasa vasorum adds local tissue hypoxia. This activates hypoxia-inducible factor-1 α (HIF-1 α) and drives excess secretion of transforming growth factor-beta (TGF- β), platelet-derived growth factor (PDGF), and basic fibroblast growth factor (bFGF).^{35,38} Diabetic vessels then thicken inward. They do not dilate. Concentric neointimal hyperplasia develops as contractile VSMCs shift into migratory, secretory osteochondrogenic myofibroblasts, and dense collagen deposition and adventitial fibrosis accompany it.^{35,38} These mechanisms from the literature could explain the smaller mean diameter of 1.74 mm in our diabetic cohort, but none was measured here.^{43,47}

Access flow volume

One finding needs comment. Access blood flow volume tended to be higher in diabetic patients than in non-diabetic controls (3489 ± 1018 vs. 3063 ± 945 mL/min, $p = 0.072$), although the difference was not significant. This occurred alongside a clearly reduced lumen caliber.¹² In fluid mechanics, volumetric flow rate (Q) through a tube is the product of mean velocity and cross-sectional area (continuity equation, $Q = v \times A$, with $A = \pi \times [d/2]^2$), while Poiseuille's equation relates flow to the pressure gradient and the fourth power of the radius.^{12,47} If an autogenous fistula narrows locally, flow conservation requires the linear velocity to rise sharply through the constriction. Laminar flow becomes a high-velocity, turbulent jet.^{12,47} Doppler ultrasound measures this fast jet in a narrow lumen, and the time-averaged velocity can then give a high

calculated flow volume.⁴⁷ Such a state may be harmful rather than a sign of healthy maturation.¹² Turbulent jet flow generates high oscillatory shear stress and boundary layer separation just downstream of the stenosis. This injures the venous endothelium and downregulates the shear-responsive transcription factor Krüppel-like factor 2 (KLF2). Post-stenotic neointimal hyperplasia and venous wall thrombosis follow.^{12,38} Very high flow through a fistula also overloads the heart. Cardiac output increases, eccentric left ventricular remodeling worsens, and high-output heart failure becomes more likely.^{12,36}

Renal resistive index in end-stage kidney disease

Doppler examination of the native interlobar and arcuate renal arteries gave a uniformly raised resistive index (RI) in every subject, with mean values of 0.825 in diabetic and 0.818 in non-diabetic patients ($p = 0.341$).⁴⁵ Outside dialysis, an RI above 0.70 is a sensitive early biomarker of diabetic microvascular nephropathy. It correlates with microalbuminuria, histopathological arteriolosclerosis, and falling glomerular filtration rate.^{45,46} In prevalent hemodialysis patients, however, the native kidneys are shrunk, fibrotic, non-functioning end-organs. They show near-total glomerulosclerosis, diffuse tubular atrophy, interstitial fibrosis, and widespread loss of microcirculation.^{7,9} With such structural destruction, intrarenal vascular resistance is irreversibly raised to near-maximal levels.⁴⁵ Systemic arterial pulse pressure and compliance also influence renal resistive index. Marked systemic arterial stiffness, present in all dialysis patients, amplifies systolic pressure peaks and depresses diastolic flow. RI values then rise independently of acute glycemic control.⁴⁵ Once end-stage parenchymal obliteration has occurred, a further difference in renal resistive index attributable to diabetes may be undetectable.

Comparison with previous studies

Our findings agree with, and extend, observations from major vascular access studies.^{43,51,52} The prospective multicenter Hemodialysis Fistula Maturation (HFM) study enrolled 602 patients at North American academic nephrology centers. In it, diabetes mellitus was one of the strongest independent predictors of unassisted fistula failure. Diabetic vessels had smaller pre-operative and post-operative cephalic vein diameters and clearly weaker outward flow-mediated dilation.^{51,52} The international Dialysis Outcomes and Practice Patterns Study (DOPPS), which covered cohorts in Europe, North America, and Japan, has repeatedly documented shorter primary unassisted fistula patency in diabetic hemodialysis patients. These patients more often needed endovascular balloon angioplasty or surgical revision, or lost the radiocephalic access altogether and moved to prosthetic grafts or central venous catheters.⁵³ Our study is consistent with these observations in a Southeast Asian hemodialysis population, and the

smaller caliber occurred without any glycemic difference in central aortic stiffness.

Measurement considerations

Careful standardization is needed to measure pulse wave velocity and vessel dimensions non-invasively.^{25,27} In our study, cfPWV averaged 2.89 ± 0.57 m/s and faPWV averaged 3.34 ± 0.73 m/s. These values are transit-time Doppler velocities. They were calculated from the subtracted surface distance between the carotid and femoral sites divided by the ECG-gated delay time, and one blinded operator acquired them with high-resolution ultrasound.^{25,26} Tonometric devices that use direct surface distance usually report aortic PWV of 7.0 to 12.0 m/s in ESKD populations. Ultrasound-derived transit velocities rely on different geometric path calculations, which give lower absolute ranges. Within a cohort, they still allow valid, precise, and reproducible comparison.²⁷ All examinations were done under identical environmental conditions, at standardized mid-week non-dialysis intervals, and by one blinded operator, so a procedural artifact is less likely, although systematic measurement error cannot be excluded.

Clinical implications

These findings matter for nephrologists, vascular surgeons, and interventional radiologists who care for chronic dialysis patients.^{36,47} First, systemic arterial stiffness measures, such as pulse wave velocity or systemic blood pressure, may say little about whether peripheral vascular access is morphologically adequate or likely to mature.^{25,36} A diabetic patient with the same cfPWV as a non-diabetic peer can still have a smaller fistula caliber.⁴³ Second, preoperative vascular Doppler ultrasound mapping should be part of standard clinical pathways for all CKD patients approaching dialysis, and especially those with diabetes.^{36,47} Guidelines recommend minimum internal lumen diameters of ≥ 2.0 mm for the inflow radial artery and ≥ 2.5 - 3.0 mm for the outflow cephalic vein before a radiocephalic fistula is attempted.^{36,47} The post-creation diameter in our diabetic cohort was smaller (1.74 mm). Surgeons evaluating diabetic candidates with borderline preoperative venous caliber might therefore consider other access configurations, such as brachiocephalic or brachio basilic transposition fistulas. They could also use pharmacoprotective strategies (for example local adventitial delivery of anti-proliferative agents or shear-stress-optimizing surgical techniques) to prevent maturation failure.^{35,38} Third, hemodialysis units should set up routine post-creation Doppler surveillance. This would detect early anastomotic and juxta-anastomotic neointimal hyperplasia in diabetic patients and allow preemptive balloon angioplasty before irreversible access thrombosis occurs.^{36,47}

Strengths

Several vascular levels were measured at once, in a well-characterized cohort of 120 prevalent

hemodialysis patients. It covered central macrovascular elastic properties (cfPWV), peripheral conduit arterial compliance (faPWV), end-organ microvascular resistance (renal RI), and the dimensions of the surgically created vascular access (fistula diameter and volume flow). One experienced vascular ultrasonographer made all measurements. This operator was blinded to glycemic status, so inter-observer variability does not arise; intra-observer reproducibility was not reported. The results are presented with exact confidence intervals and standardized effect sizes.

Limitations

Several limitations apply. First, the design was cross-sectional and observational, so it does not allow inference about longitudinal causal trajectories between glycemic exposure and progressive luminal narrowing. Second, no sample-size calculation was done, so the study may have been underpowered for small to medium effects in the 22-patient diabetic subgroup (the fistula diameter difference had Cohen's $d = -0.86$). The diabetic subgroup had only 22 patients (18.33%), which reflects the consecutive distribution of diabetic nephropathy at this regional tertiary center. Third, cumulative glycemic control (longitudinal HbA1c or glycated albumin) and circulating markers of mineral-bone disorder were not systematically available for multivariable adjustment. These markers include intact parathyroid hormone, fibroblast growth factor-23, soluble Klotho, fetuin-A, and uncarboxylated matrix Gla protein. Fourth, access maturation was assessed once and was not followed serially from the day of surgical creation. Fifth, age and sex differed between the groups (female 72.7% vs. 40.8%), no adjusted analysis was performed, and the study was done at a single center. Sixth, time since fistula creation, preoperative vessel size and intra-observer reproducibility were not recorded, and the cfPWV, diameter and flow values require verification against the source records.

Future directions

Future work should build on these findings. Multicenter prospective longitudinal cohorts are the next step. They should follow diabetic and non-diabetic CKD patients from preoperative vascular mapping through surgical creation and maturation, and over several years of dialysis. Serial high-resolution intravascular ultrasound (IVUS) or optical coherence tomography (OCT) could be combined with circulating multi-omics panels (microRNAs, inflammatory cytokines, and CKD-MBD regulators). Such work would help identify the molecular switches that favor inward neointimal hyperplasia over outward eutrophic remodeling. Randomized trials of targeted drugs are needed too. Their goal would be to protect access longevity in diabetic hemodialysis patients, and candidates include local perivascular sustained-release

sirolimus wraps, endothelial-protective SGLT2 inhibitors, and advanced glycation cross-link breakers.

5. Conclusion

Central aortic stiffness (cfPWV), peripheral arterial stiffness (faPWV), and native renal resistive index (RI) did not differ significantly between diabetic and non-diabetic individuals in this cohort of 120 prevalent maintenance hemodialysis patients. A ceiling set by uremic retention, Mönckeberg medial calcinosis, and mineral-bone disorder may explain this. This hypothesis was not tested.

Radiocephalic AVF caliber, by contrast, was smaller in diabetic patients (1.74 ± 0.63 mm vs. 2.36 ± 0.74 mm, $p < 0.001$; Cohen's $d = -0.86$), and volume flow was numerically higher but not significantly so. Diabetes was therefore associated with a smaller fistula caliber. Remodeling, fibrosis, and neointimal hyperplasia were not measured. Preoperative vascular mapping and Doppler surveillance of access caliber deserve consideration in diabetic patients. Longitudinal studies must show whether they protect access longevity.

In conclusion, central and access findings diverged in these patients. Central arterial stiffness did not differ by glycemic status, possibly because of a ceiling set by end-stage uremic calcification. Diabetes was associated with a smaller caliber of the peripheral access. Systemic stiffness may not predict access health at all. Targeted Doppler surveillance and proactive surgical planning should be considered to protect the vascular lifeline of diabetic hemodialysis patients.

Declarations

Ethics approval and consent to participate

The study protocol conformed to the ethical principles of the Declaration of Helsinki and was reviewed and approved by the Ethics Committee CMHC Research Center Indonesia (Reference number 2024/297). Written informed consent was obtained from all participants before enrollment.

Consent for publication

All participants provided informed consent for the publication of anonymized research data and associated medical imaging metrics.

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Conflicts of interest

The authors declare that they have no competing financial, personal, or professional interests that could have influenced the work reported in this manuscript.

Author contributions

H.H.: conceptualization, methodology, investigation, supervision, writing – review & editing. G.P.D.: investigation, resources, data curation. E.V.: investigation, data curation, project administration.

M.R.F.: formal analysis, software, visualization, writing – original draft. All authors reviewed and approved the final manuscript.

Data availability

The de-identified numerical datasets, Doppler ultrasound measurements, and analytical code generated during the study are available from the corresponding author on reasonable academic request.

Generative AI disclosure

None. Generative artificial intelligence tools were not used in the preparation of this manuscript.

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