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Weight-Based Assessment of Access Flow Threshold to Predict Arteriovenous Fistula Functional Patency

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Introduction: The 2019 Kidney Disease Outcome Quality Initiative (K/DOQI) guideline recommended evaluating arteriovenous fistula (AVF) malfunction risks primarily based on clinical monitoring, which can be assisted with the value of vascular access flow (Qa). Nevertheless, Qa thresholds recommended by different guidelines vary, ranging from 300 to 500 ml/min. This study investigated the optimal Qa threshold to predict future functional patency in AVFs with Qa <500 ml/min.

Methods: Both the clinical indicators of access dysfunction and the Qa value were monitored in patients receiving hemodialysis by the radiocephalic AVF. Routine access flow surveillance was performed by the ultrasound dilution method (HD03, Transonic Inc.). The development of clinically significant indicators of access dysfunction, which necessitated percutaneous transluminal angiography (PTA) to maintain functional patency, was analyzed in this cohort.

Results: Among the enrolled 302 patients, Qa of 52 patients was under 500 ml/min. These 52 patients received 2 Qa measurements during the follow-up period. Of these 52 patients, serial Qa of 17 patients varied trivially and their AVF remained functional. Multivariable logistic regression analysis revealed that a low Qa per ideal body weight (IBW) is an independent predictor of AVF functional loss. Receiver operating characteristic curve analysis of Qa/IBW in predicting future AVF functional loss revealed that the best cutoff value of Qa is 7.1 times the IBW.

Conclusion: For radiocephalic AVFs with Qa <500 ml/min, the minimally required Qa to maintain access function is associated with individual IBW. The IBW-based Qa threshold assessment would allow more flexibility in the treatment of patients and reduce unnecessary invasive measures.

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Vascular access is the lifeline for patients with hemodialysis.[1] AVF provides superior patency than arteriovenous graft or tunneled catheters.[2] Yet, the provision of good quality access, even with AVF, remains challenging to achieve owing to foreseeable stenosis leading to thrombosis. Monitoring AV fistulae and grafts for hemodynamically significant stenosis improved patency and outcome in conjunction with corrective treatment.[3–6] Nevertheless, this proactive approach might increase the likelihood of overdoing pre-emptive measures and may lead to unintended vascular damage.[7]

The 2019 National Kidney Foundation's K/DOQI guideline recommended evaluating AVF malfunction risks based mainly on clinical monitoring, rather than solely relying on Qa alone.[8] Regarding the optimal Qa threshold, the K/DOQI guideline indicated that those with AVF access flow rate <500 ml/min, arteriovenous graft access flow rate <600 ml/min, or access flow rate

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Table 1. Characteristics of patients on dialysis whose AVFs remained functionally patent or not throughout the follow-up period

Factor	Functional patency: Yes [PTA_1 (−) and PTA_2 (−)]	Functional patency: No [PTA_1 (+) or PTA_2 (+)]	*p* value
Patient number (*n*)	17	35	
Age (yr)	75.8 ± 12.6	70.4 ± 12.5	0.152
Male gender (*n*; %)	7; 41.2	20; 57.1	0.280
Dialysis duration (mo)	55.9 ± 47.8	33.2 ± 21.5	0.077[a]
BH (cm)	157.6 ± 7.2	162.5 ± 6.9	0.023[b]
Actual BW (kg)	57.9 ± 10.6	63.6 ± 12.0	0.105
BMI (kg/m^2)	23.3 ± 3.9	24.0 ± 4.0	0.554
BSA (m^2)	1.59 ± 0.16	1.69 ± 0.18	0.061[a]
Ideal BW (kg)	52.1 ± 7.8	57.2 ± 8.2	0.036[b]
Adjusted BW (kg)	52.7 ± 7.4	57.3 ± 9.0	0.071[a]
Access flow			
Qa_1 (ml/min)	426.5 ± 81.9	328.3 ± 117.0	0.001[c]
Qa_2 (ml/min)	508.8 ± 245.5	785.4 ± 386.7	0.003[c]
Comorbidities			
Diabetes mellitus (*n*; %)	6; 35.3	8; 22.9	0.506
Hypertension (*n*; %)	9; 52.9	24; 68.6	0.272
Congestive heart failure (*n*; %)	4; 23.5	4; 11.4	0.257
Ischemic heart disease (*n*; %)	3; 17.6	3; 8.6	0.379
Cerebrovascular disease (*n*; %)	0; 0.0	1; 2.9	1.000
Biochemical data			
Albumin (g/dl)	3.7 ± 0.3	3.9 ± 0.3	0.091[a]
Cholesterol (mg/dl)	155.4 ± 42.1	162.9 ± 35.3	0.504
Triglycerides (mg/dl)	185.0 ± 123.1	198.1 ± 151.8	0.759
Uric acid (mg/dl)	6.3 ± 1.9	7.2 ± 2.5	0.195
Fasting glucose (mg/dl)	153.4 ± 102.9	147.0 ± 76.1	0.801
Total bilirubin (mg/dl)	0.7 ± 0.3	0.6 ± 0.2	0.270
ALT (U/l)	13.8 ± 7.4	11.9 ± 5.2	0.292
AST (U/l)	18.4 ± 6.9	16.1 ± 6.3	0.245
Calcium (mg/dl)	9.4 ± 0.7	9.4 ± 0.9	0.861
Phosphate (mg/dl)	4.4 ± 1.4	4.9 ± 1.2	0.194
ALP (mg/dl)	105.8 ± 60.7	76.3 ± 36.3	0.040[b]
Intact PTH (pg/ml)	427.9 ± 355.4	309.9 ± 277.8	0.196
WBC count (1000/cumm)	6.3 ± 1.5	6.3 ± 1.4	0.990
Hemoglobin (g/dl)	10.2 ± 1.0	10.1 ± 1.5	0.692
Platelet count (1000/cumm)	153.7 ± 49.8	178.8 ± 44.2	0.071[a]
Hemodialysis parameters			
IDWG/BW (%)	4.0 ± 1.3	3.7 ± 1.2	0.452
Qb (ml/min)	252.8 ± 24.5	252.4 ± 32.4	0.966
Qb/Qa_1 (%)	62.0 ± 16.6	90.3 ± 42.8	0.001[c]
Qa_1/BH (ml/min/m)	271.9 ± 56.9	201.3 ± 69.9	0.001[c]
Qa_1/actual BW (ml/min/kg)	7.6 ± 2.0	5.3 ± 2.3	0.001[c]
Qa_1/BMI (ml× m^2/min/kg)	18.7 ± 4.4	14.2 ± 6.1	0.015[b]
Qa_1/BSA (ml/min/m^2)	272.1 ± 61.9	195.9 ± 72.7	0.003[c]
Qa_1/ideal BW (ml/min/kg)	8.4 ± 2.3	5.8 ± 2.0	0.001[c]
Qa_1/adjusted BW (ml/min/kg)	8.3 ± 2.1	5.8 ± 2.3	0.003[c]

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; AVF, arteriovenous fistula; BH, body height; BMI, body mass index; BSA, body surface area; BW, body weight; IDWG, interdialytic weight gain; PTA_1, percutaneous transluminal angioplasty after the Qa_1 measurement; PTA_2, percutaneous transluminal angioplasty after the Qa_2 measurement; PTH, parathyroid hormone; Qa_1, the initial access flow; Qa_2, the subsequent access flow; Qb, blood pump flow; WBC, white blood cell count.
[a] $P < 0.10$.
[b] $P < 0.05$.
[c] $P < 0.01$.
Values are expressed as mean ± SD.

decline 25% in 3 to 6 months possess a higher risk of stenosis or thrombosis.[3] In contrary, the Renal Association Clinical Practice Guidelines on Vascular Access for Hemodialysis recommended an access flow rate of <300 ml/min as the standard for intervention.[5] Additional corresponding studies suggested an intermediate threshold of 350 ml/min in predicting incipient thrombosis.[9,10] In short, the Qa thresholds recommended by the guidelines vary, ranging from Qa <500 to Qa <300 ml/min.[3–6,11] In addition, for patients whose AVF was mature, their Qa value is positively associated with the overweight status.[12] This

observation suggests that a single Qa threshold for angiography in all patients may be too simplistic and that the optimal Qa threshold might be different among patient subgroups.[12]

Nevertheless, none of the above-mentioned studies on optimal Qa thresholds evaluated Qa/body size as a ratio in predicting future AVF outcomes in each cohort. Considering that significantly higher Qa was observed in overweight patients,[12] we hypothesized that patients with lower body size require less access flow, thus have a lower Qa cutoff value for intervention. Therefore, we conducted this study to determine the minimally required Qa that maintains a functioning AVF and whether body size indicators contribute to the prediction of future functional patency.

METHODS

Study Participants

From April 2020 to March 2021, a total of 359 subjects under maintenance hemodialysis by the radiocephalic AVF for >3 months were eligible for this study. The initial Qa (Qa_1) of the participants was measured and documented. The cutoff point of Qa_1 was set at 500 ml/min as recommended by the K/DOQI guideline,[3] where subjects below this standard but without any clinical indicator of access dysfunction were included for outcome analysis. The body weight (BW) was defined as the postdialytic BW at the study entry. The Institutional Review Board approved all protocols of the institute before the study began, and the protocols conformed to the ethical guidelines of the Helsinki Declaration. The need for informed consent was waived by the Institutional Review Board of the institute given the study's retrospective nature, and all the procedures being performed were part of the routine care.

Study Design

In this cohort, routine Qa surveillance was performed quarterly by the ultrasound dilution method (HD03, Transonic Inc., Ithaca, NY) within 2 hours after dialysis initiation. The subjects were separated into 2 groups according to their Qa_1 cutoff value set at 500 ml/min. Among patients with Qa_1 of <500 ml/min, those with clinical indicators of access dysfunction were excluded. The remaining were closely monitored for the development of clinical indicators of access dysfunction.

This study aims to identify the optimal Qa threshold to predict future functional patency to reduce unnecessary intervention procedures. Second, the authors aim to evaluate whether BW is a determining factor in predicting the functional patency of vascular access. In addition to actual BW, they also evaluated the predictive values of other body size indicators, including body height (BH), body mass index, body surface area (body surface area $= \sqrt{}$ [BH [cm] × BW [kg] ÷ 3600]),[13] IBW (male, 50 [kg] + (BH [cm] - 152.4) × 0.91; female, 45.5 [kg] + (BH [cm] - 152.4) × 0.91),[14] and adjusted BW (AdjBW) (if actual BW > ideal BW, AdjBW = ideal BW + 0.25 × (actual BW - ideal BW); if actual BW < ideal BW, AdjBW = actual BW)[15] according to previous literature.

Clinical Outcomes

Functional patency of AVF is the primary decisive factor of adequate dialysis, as defined by a functioning AVF able to provide enough access flow for 4 hours of adequate dialysis delivery.[16,17] Access dysfunction is defined as the development of clinical signs and symptoms that suggest underlying clinically significant lesions.[8] In these cases, PTA therapy was necessitated to maintain functional access.

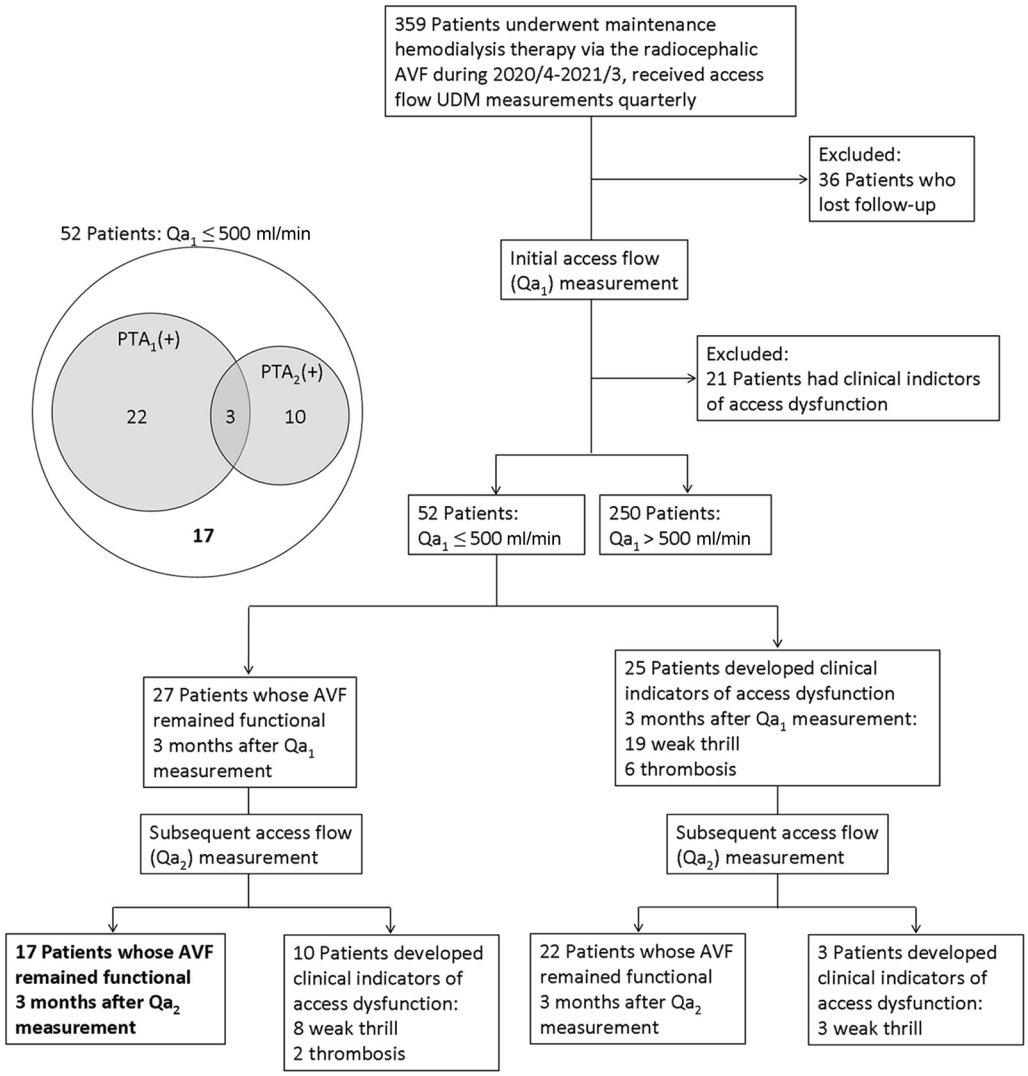
Statistical Analysis

χ^2 analysis or Fisher's exact test was used for comparisons of categorical variables as appropriate. Continuous variables were compared by *t* test or paired *t* test as appropriate. The continuous variables are presented as mean and SD unless otherwise specified. To confirm the independent predictors of AVF functional loss, we used multivariable logistic regression analysis. A propensity score was generated and included in the multivariable logistic regression analysis to avoid model overfitting in view of the relatively small size of the present cohort. The propensity score was calculated using a logistic model consisting of possible confounding variables. Age, sex, and Table 1 variables with a $P < 0.10$ were included for the propensity score generation, that is, dialysis duration, albumin, alkaline phosphatase, and platelet count. The multivariable logistic regression analysis included factors with a $P < 0.01$ in the univariate adjusted model. Receiver operating characteristic curve analyses were performed to determine the best cutoff values, at which the square root value of the sum of $(1 - \text{sensitivity})^2$ and $(1 - \text{specificity})^2$ is the minimum,[18] for predicting the Qa per kilogram IBW that is sufficient to maintain a functional AVF. Statistical Package for the Social Sciences version 18.0 (SPSS Inc., Chicago, IL) was used for all statistical analyses. All probabilities were 2-tailed, and a $P < 0.05$ was considered statistically significant.

RESULTS

Demographic Characteristics of Study Participants

From April 2020 to March 2021, a total of 2 separate Qa measurements (Qa_1 and Qa_2) were performed at a 3-month interval. Figure 1 reveals the study flow of the eligible 359 patients, 36 of whom were excluded owing to lack of



52 Patients: $Qa_1 \leq 500$ ml/min

PTA_1	PTA_2	Patient number (*n*)	BH (cm)	Actual BW (kg)	BMI (kg/m^2)	BSA (m^2)	Ideal BW (kg)	Adjusted BW (kg)
(-)	**(-)**	**17**	**157.6 ± 7.2**	**57.9 ± 10.6**	**23.3 ± 3.9**	**1.59 ± 0.16**	**52.1 ± 7.8**	**52.7 ± 7.4**
(-)	(+)	10	163.2 ± 7.7	67.6 ± 8.9	25.4 ± 2.9	1.75 ± 0.14	58.5 ± 9.0	60.0 ± 7.9
(+)	(-)	22	162.6 ± 6.5	61.1 ± 11.9	23.1 ± 4.2	1.65 ± 0.18	57.2 ± 7.7	56.2 ± 9.0
(+)	(+)	3	159.2 ± 9.6	67.8 ± 20.6	26.3 ± 4.7	1.72 ± 0.31	53.2 ± 11.3	56.8 ± 13.6

Figure 1. Flow diagram for the study. Among the 52 patients whose access flow was <500 ml/min, 17 remained free of symptomatic AVF stenosis or thrombosis during a mean follow-up period of 5.9 months. AVF, arteriovenous fistula; BH, body height; BMI, body mass index; BSA, body surface area; BW, body weight; PTA_1, percutaneous transluminal angioplasty after the Qa_1 measurement; PTA_2, percutaneous transluminal angioplasty after the Qa_2 measurement; Qa_1, the initial access flow; Qa_2, the subsequent access flow; UDM, ultrasound dilution method.

complete data. A further 21 patients were excluded because they had clinical indicators of access dysfunction. Eventually, 302 patients without clinical indicators of access dysfunction were included in this study. Among them, 250 subjects had Qa_1 >500 ml/min ($Qa_1 = 1361.6 \pm 551.6$ ml/min), whereas Qa_1 of the remaining 52 patients was <500 ml/min ($Qa_1 = 360.4 \pm 115.7$ ml/min) (Table 2).

Clinical Indicators of Access Dysfunction

As found in Supplementary Table S1, of the remaining 52 patients, 25 developed clinically significant stenosis or thrombosis within 3 months after the Qa_1 measurement, which necessitated PTA (PTA_1 [+]). After PTA_1, their access flow rate increased from 341.2 ± 105.3 ml/min (Qa_1) to 934.0 ± 352.5 ml/min (Qa_2) within the next 3 months ($P < 0.001$).

The remaining 27 patients with asymptomatic AVF were also subjected to a subsequent Qa measurement (Qa_2) 3 months after Qa_1 measurement. Three months after the Qa_2 measurement, 17 patients remained asymptomatic [(PTA_1 [−] and PTA_2 [−]], whereas PTA was necessitated in the remaining 10 patients (PTA_2 [+]).

Table 2. Characteristics of patients on dialysis with Qa_1 >500 ml/min versus Qa_1 ≤500 ml/min

Factor	Qa_1 >500 ml/min	Qa_1 ≤500 ml/min	*P* value
Patient number (*n*)	250	52	
Age (yr)	62.4 ± 15.8	72.2 ± 12.7	<0.001[a]
Male gender (*n*; %)	153; 61.2	27; 51.9	0.215
Dialysis duration (mo)	62.1 ± 106.1	40.6 ± 33.8	0.009[a]
BH (cm)	162.7 ± 8.4	160.9 ± 7.3	0.142
Actual BW (kg)	63.2 ± 14.1	61.7 ± 11.8	0.480
BMI (kg/m^2)	23.7 ± 4.4	23.8 ± 4.0	0.949
BSA (m^2)	1.68 ± 0.21	1.65 ± 0.18	0.389
Ideal BW (kg)	57.6 ± 9.3	55.5 ± 8.3	0.132
Adjusted BW (kg)	57.5 ± 9.9	55.8 ± 8.7	0.273
Access flow			
Qa_1 (ml/min)	1361.6 ± 551.6	360.4 ± 115.7	<0.001[a]
Comorbidities			
Diabetes mellitus (*n*; %)	68; 27.2	14; 26.9	0.967
Hypertension (*n*; %)	147; 58.8	33; 63.5	0.533
Congestive heart failure (*n*; %)	33; 13.2	8; 15.4	0.676
Ischemic heart disease (*n*; %)	20; 8.0	6; 11.5	0.416
Cerebrovascular disease (*n*; %)	9; 3.6	1; 1.9	1.000
Biochemical data			
Albumin (g/dl)	3.9 ± 0.3	3.8 ± 0.3	0.103
Cholesterol (mg/dl)	171.2 ± 41.7	160.4 ± 37.4	0.087
Triglycerides (mg/dl)	185.0 ± 123.1	191.6 ± 160.0	0.905
Uric acid (mg/dl)	6.8 ± 4.0	6.9 ± 2.3	0.831
Fasting glucose (mg/dl)	136.9 ± 64.4	149.1 ± 84.8	0.243
Total bilirubin (mg/dl)	0.6 ± 0.3	0.7 ± 0.2	0.857
ALT (U/l)	14.4 ± 9.8	12.6 ± 6.0	0.086
AST (U/l)	18.2 ± 9.8	16.9 ± 6.6	0.372
Calcium (mg/dl)	9.3 ± 0.9	9.4 ± 0.8	0.347
Phosphate (mg/dl)	5.1 ± 1.4	4.7 ± 1.3	0.070
ALP (mg/dl)	114.6 ± 141.3	91.6 ± 52.2	0.249
Intact PTH (pg/ml)	498.1 ± 519.5	348.5 ± 306.9	0.006[a]
WBC count (1000/mm^3)	6.2 ± 2.8	6.3 ± 1.4	0.850
Hemoglobin (g/dl)	10.3 ± 1.2	10.1 ± 1.3	0.489
Platelet count (1000/mm^3)	175.7 ± 56.1	170.6 ± 447.1	0.545
Hemodialysis parameters			
Urea reduction rate (%)	74.0 ± 6.0	75.3 ± 4.5	0.134
Kt/V	1.6 ± 0.3	1.6 ± 0.6	0.781
nPCR (g/kg/d)	1.4 ± 0.4	1.4 ± 0.3	0.540
TACurea (mg/dl)	49.3 ± 12.9	49.5 ± 13.2	0.923

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BH, body height; BMI, body mass index; BSA, body surface area; BW, body weight; KT/V, (Kurea × Td)/Vurea; nPCR, normalized protein catabolic rate; PTH, parathyroid hormone; Qa_1, the initial access flow; TACurea, time-averaged concentration of blood urea nitrogen; WBC, white blood cell count.
[a]$P < 0.05$.
Values are expressed as mean ± SD.

Qa per IBW Is an Independent Predictor of AVF Functional Loss

Table 1 compares the 17 patients who never received PTA during the follow-up period with another 35 patients who required PTA at least once to maintain functional patency. The 17 patients who did not require any PTA had significantly higher Qa/BH, Qa/actual BW, Qa/body mass index, Qa/body surface area, Qa/IBW, and Qa/AdjBW than those who experienced AVF functional loss. There was no difference in blood pump speed (Qb) between the 2 groups. The time interval between Qa_1 and Qa_2 was 3.1 ± 1.5 months, with 3.1 ± 1.1 months for the 17 patients who received no PTA treatment and 3.1 ± 1.6 months for the 35 patients who developed access dysfunction. The time interval between Qa_1 and Qa_2 had no effect on the outcome ($P = 0.936$). Supplementary Table S2 evaluating the PTA-free group ($n = 17$) and patients who necessitated PTA_2 ($n = 10$) reveals similar results.

Table 3 reveals the multivariable logistic regression analysis results of independent predictors of AVF functional loss. After adjusting for confounding factors, Qa alone, Qb/Qa, Qa/BH, Qa/actual BW, Qa/body mass index, Qa/body surface area, Qa/IBW, and Qa/AdjBW are still statistically significant predictors of AVF functional loss in the univariate logistic regression analysis. Further multivariable logistic regression analysis of the adjusted model revealed that Qa/IBW is the only factor that remains statistically significant. Next, the receiver operating characteristic analyses revealed that the area under the curves (AUCs) of Qa/IBW (AUC: 0.813) and Qa/BH (AUC: 0.803) outperform the AUCs of Qa/actual BW (AUC: 0.788), Qa alone (AUC 0.761), and Qa/body mass index (AUC 0.745) (Supplementary Table S3), among which Qa/IBW yielded the highest AUC value. The receiver operating characteristic curve analysis revealed that the best cutoff value of Qa/IBW was 7.1, meaning that a Qa >7.1 times the IBW predicts future functional patency in radiocephalic AVFs (Figure 2). The diagnostic performance of Qa/IBW was 76.5% sensitivity, 74.3% specificity, 75.0% accuracy, 59.1% positive predictive value, and 86.7% negative predictive value. In contrast, the diagnostic performance of Qa alone was 76.5% sensitivity, 62.9% specificity, 67.3% accuracy, 50.0% positive predictive value, and 84.6% negative predictive value.

DISCUSSION

Through clinical monitoring and Qa surveillance, our study revealed a minimally required Qa for a functioning radiocephalic AVF. Below that value, the AVF is more likely to experience future functional loss. Our results apply to radiocephalic AVFs with Qa <500 ml/min. Furthermore, we identified that such minimally required access flow depends on the individual body size. Qa/IBW outperforms other body size indicators and remains a significant determinant of AVF functionality in multivariable analysis. Although providing greater flexibility and custom treatment for each patient, IBW is an easily obtainable value that can be easily applied in a clinical setting.

On the basis of previous evidence,[9,10,16] 2 guidelines recommended a threshold of Qa <300 to 350 ml/min to

Table 3. Crude and adjusted logistic regression analysis of significant predictors of arteriovenous fistula functional loss

	Univariate								Multivariable			
		95% CI				95% CI				95% CI		
Factor	Crude OR	Lower	Upper	*P* value	Adjusted OR[a]	Lower	Upper	*P* value	Adjusted OR[a]	Lower	Upper	*P* value
Qa_1 (ml/min)	0.990	0.983	0.997	0.009[b]	0.987	0.977	0.997	0.008[b]				
Qb/Qa_1 (%)	1.038	1.004	1.074	0.030[c]	1.042	1.003	1.081	0.033[c]				
Qa_1/BH (ml/min/m)	0.982	0.969	0.994	0.004[b]	0.978	0.963	0.993	0.005[b]				
Qa_1/actual BW (ml/min/kg)	0.636	0.465	0.868	0.004[b]	0.607	0.410	0.896	0.012[c]				
Qa_1/BMI (ml × m^2/min/kg)	0.864	0.768	0.972	0.015[c]	0.830	0.709	0.973	0.022[c]				
Qa_1/BSA (ml/min/m^2)	0.984	0.973	0.994	0.003[b]	0.981	0.968	0.995	0.006[b]				
Qa_1/ideal BW (ml/min/kg)	0.558	0.392	0.795	0.001[b]	0.535	0.348	0.823	0.004[b]	0.535	0.348	0.823	0.004[b]
Qa_1/adjusted BW (ml/min/kg)	0.613	0.444	0.845	0.003[b]	0.601	0.407	0.887	0.010[c]				

BH, body height; BMI, body mass index; BSA, body surface area; BW, body weight; OR, odds ratio; Qa_1, the initial access flow; Qb, blood pump flow.
[a]Adjusted models were adjusted for a propensity score consisting of factors with a $P < 0.10$ in Table 1, including dialysis duration, albumin, alkaline phosphatase, and platelet count. Factors with a $P < 0.01$ in the univariate adjusted model were included in the multivariable logistic regression analysis.
[b]$P < 0.01$.
[c]$P < 0.05$.

predict AVF stenosis.[5,6] In our study, the Qa threshold, that is, 7.1 times the IBW, while applying the average IBW value in our cohort (Table 1), ranges from 370 to 406 ml/min. Such IBW-based assessment of the Qa threshold is close to those reported previously.[9,10,16] As the IBW is calculated from BH but not BW,[14] this reflects our findings revealing Qa/IBW and Qa/BH have higher predictive power on AVF functionality than the Qa/actual BW. Although the data regarding upper limb vessels are lacking, it has been reported that the carotid and femoral vessels were positively correlated with individual BH.[19–22] Moreover, the BH was also positively associated with cardiac output.[23] Therefore, it makes sense that patients with smaller body sizes might require less Qa to maintain AVF functionality.

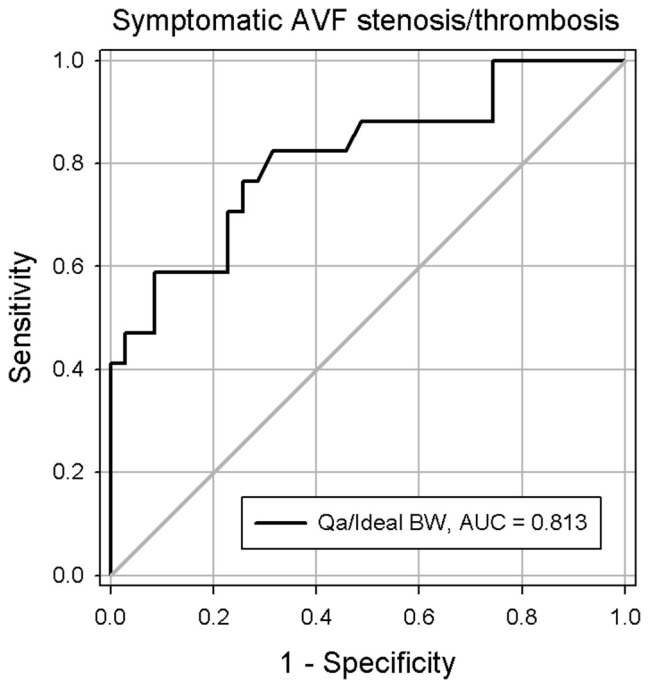


Figure 2. Receiver operating characteristic curves of Qa per ideal BW in predicting symptomatic stenosis/thrombosis of radiocephalic arteriovenous fistulae. The best cutoff value of Qa for predicting clinically significant stenosis/thrombosis is 7.1 times the ideal BW, with an AUC of 0.813. AUC, area under the curve; AVF, arteriovenous fistula; BW, body weight; Qa, access flow.

As illustrated in Supplementary Table S3, the AUC of Qa/IBW is higher than that of Qa/BH. This might be partly explained by the fact that as compared with Qa/BH, Qa/IBW further contains the information of gender differences.[14] As illustrated in Table 1, in the group of 17 patients maintaining patency, the prevalence of females (58.8%) was greater than those who did not (42.9%), though not statistically different. The diameter of the radial artery, the inflow vessel of the radiocephalic fistula, has been reported to be significantly larger in males than in females.[24–26] As a result, females might require less Qa than males to maintain their AVF functionality, necessitating further large-scale studies to confirm.

The inconsistent threshold values in different guidelines suggest that existing guidelines do not account for clinical variables other than stenosis that can affect the Qa value. Factors that might influence access provision and survival include but are not limited to diabetes mellitus and the presence of previous or current arterial vascular disease. Selective accountment of the different factors may be required for a timely and correct response to a failing fistula. Patient weight is a determining factor for AVF patency while also easily accessible in clinical practice. Although obese patients on hemodialysis are less likely to receive an AVF,[27,28] for patients whose AVF was mature, their Qa is positively associated with the overweight status.[12] Patients with greater IBW may be more susceptible to reduced patency than their counterparts while simultaneously requiring much higher Qa for regular function.[27,29] These observations partly support our findings, indicating the minimally required Qa for an uneventful hemodialysis therapy is 7.1 times the IBW. Greater

weight is an independent factor associated with an increased need for intervention, whereas the equivalent Qa is sufficient for patients with lower IBW to deliver adequate dialysis doses.

The 2019 K/DOQI guideline emphasized the importance of clinical monitoring rather than Qa value alone.[8] Such recommendation was primarily based on a large Medicare cohort consisted of 35,716 subjects, revealing that the 1-year AVF patency was not significantly different between the preventive PTA group and matched controls.[30] Besides, a prospective randomized controlled trial angiographically treated patients with a Qa of >500 ml/min but had abnormal clinical monitoring findings. The results revealed that pre-emptive PTA was beneficial in reducing access loss.[7] Therefore, clinical judgment should not solely rely on the Qa surveillance findings.[8,31] Nevertheless, evidence has revealed that Qa surveillance provides additional values on clinical monitoring to increase the rate of detecting AVF stenosis.[32] For the 17 patients whose AVF remained functionally patent during the follow-up period in our cohort, their average initial Qa (Qa_1) was 426.5 ml/min, and the subsequent Qa (Qa_2) was 508.8 ml/min, which became >500 ml/min without any intervention. This observation suggests that though trivial the intraindividual variation of Qa exists and that clinical judgment should not be based solely on Qa surveillance data, echoing the 2019 K/DOQI recommendation.

Guidelines recommended that angiography may be considered in AVF with Qa <500 ml/min or in which Qa declines by >20%. These cutoff values were supported by observational studies.[32–39] Evidently, following the guideline might lead to the identification of subclinical stenosis, yet the reported positive predictive value is only approximately 70%.[40] In this study, we aimed to identify parameters that might increase the predictive power of screening. An adequate hemodialysis therapy relies on a sufficient Qa to provide Qb. Thus, a higher Qb-to-Qa ratio indicates that access flow is strenuous to maintain blood pump flow, as found in the 35 PTA-requiring patients of our cohort (Table 1). Nevertheless, this cannot explain the difference in Qa observed in those who necessitated PTA versus those who had a Qa lower than 500 ml/min yet sufficient flow to maintain hemodialysis treatment. We found that the 17 patients who received neither PTA_1 nor PTA_2 had a higher Qa/IBW, linking a positive relationship between a lower IBW and a reduced need for PTA intervention.

Our study has limitations. First, this is a retrospective study. Second, the present cohort only evaluated AVFs with Qa <500 ml/min. Further studies focusing on patients with Qa >500 ml/min are warranted. For patients with Qa <500 ml/min, our findings may provide additional clues for clinical judgment on the interventionist referral. Third, our results were derived from a cohort of radiocephalic AVFs, and further studies are warranted to extend this work to other sorts of fistulas. Nevertheless, we did identify that differing patient characteristics could be taken into account when setting an optimal threshold to predict radiocephalic AVF functionality.

In conclusion, the Qa threshold for a functional AVF should take IBW into consideration but not just rely on a unified cutoff value. The association between IBW and required Qa will allow more patient treatment flexibility and reduce unnecessary invasive measures.

DISCLOSURE

All the authors declared no competing interests.

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ETHICS APPROVAL

All protocols conformed to the ethical guidelines of the Helsinki Declaration. The study protocol was reviewed and approved by the Institutional Review Board of the Taipei Veterans General Hospital.

CONSENT TO PARTICIPATE

The need for informed consent was waived by the Institutional Review Board of the institute given the study's

retrospective nature, and all the procedures being performed were part of the routine care.

AUTHOR CONTRIBUTIONS

Conceptualization: CYY, YFW
Methodology: CYY, BSW, YFW
Formal analysis and investigation: CYY, BSW, YFW
Writing—original draft preparation: CYY, BSW, YFW
Writing—review and editing: CYY, YHWL, DCT
Funding acquisition: CYY, YHWL, DCT
Resources: CYY, YHWL, DCT
Supervision: CYY, YHWL, DCT

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1. Characteristics of patients on dialysis whose AVFs remained functionally patent versus those who developed clinically significant stenosis/thrombosis after the Qa_1 measurement.

Table S2. Characteristics of patients on dialysis whose AVFs remained functionally patent versus those who developed clinically significant stenosis/thrombosis after the Qa_2 measurement.

Table S3. Receiver operating characteristic curves of access flow (Qa) per body size indicators in predicting symptomatic stenosis/thrombosis of radiocephalic arteriovenous fistulae.

REFERENCES

1. Riella MC, Roy-Chaudhury P. Vascular access in haemodialysis: strengthening the Achilles' heel. *Nat Rev Nephrol*. 2013;9:348–357. https://doi.org/10.1038/nrneph.2013.76
2. Lee HS, Song YR, Kim JK, et al. Outcomes of vascular access in hemodialysis patients: analysis based on the Korean National Health Insurance Database from 2008 to 2016. *Kidney Res Clin Pract*. 2019;38:391–398. https://doi.org/10.23876/j.krcp.19.015
3. Vascular Access 2006 Work Group. Clinical practice guidelines for vascular access. *Am J Kidney Dis*. 2006;48(suppl 1):S176–S247. https://doi.org/10.1053/j.ajkd.2006.04.029
4. Jindal K, Chan CT, Deziel C, et al. Hemodialysis clinical practice guidelines for the Canadian Society of Nephrology. *J Am Soc Nephrol*. 2006;17(suppl 1):S1–S27. https://doi.org/10.1681/ASN.2005121372
5. Fluck R, Kumwenda M. Renal Association Clinical Practice Guideline on vascular access for haemodialysis. *Nephron Clin Pract*. 2011;11(suppl 1):c225–c240. https://doi.org/10.1159/000328071
6. Tordoir J, Canaud B, Haage P, et al. EBPG on vascular access. *Nephrol Dial Transplant*. 2007;22(suppl 2):ii88–ii117. https://doi.org/10.1093/ndt/gfm021
7. Tessitore N, Bedogna V, Poli A, et al. Should current criteria for detecting and repairing arteriovenous fistula stenosis be reconsidered? Interim analysis of a randomized controlled trial. *Nephrol Dial Transplant*. 2014;29:179–187. https://doi.org/10.1093/ndt/gft421
8. Lok CE, Huber TS, Lee T, et al. KDOQI clinical practice guideline for vascular access: 2019 update [published correction appears in *Am J Kidney Dis*. 2021;77:551]. *Am J Kidney Dis*. 2020;75(suppl 2):S1–S164. https://doi.org/10.1053/j.ajkd.2019.12.001
9. Tessitore N, Lipari G, Poli A, et al. Can blood flow surveillance and pre-emptive repair of subclinical stenosis prolong the useful life of arteriovenous fistulae? A randomized controlled study. *Nephrol Dial Transplant*. 2004;19:2325–2333. https://doi.org/10.1093/ndt/gfh316
10. Tessitore N, Bedogna V, Gammaro L, et al. Diagnostic accuracy of ultrasound dilution access blood flow measurement in detecting stenosis and predicting thrombosis in native forearm arteriovenous fistulae for hemodialysis. *Am J Kidney Dis*. 2003;42:331–341. https://doi.org/10.1016/s0272-6386(03)00659-0
11. Tessitore N, Bedogna V, Verlato G, Poli A. The rise and fall of access blood flow surveillance in arteriovenous fistulas. *Semin Dial*. 2014;27:108–118. https://doi.org/10.1111/sdi.12187
12. Tonelli M, Hirsch DJ, Chan CT, et al. Factors associated with access blood flow in native vessel arteriovenous fistulae. *Nephrol Dial Transplant*. 2004;19:2559–2563. https://doi.org/10.1093/ndt/gfh406
13. Mosteller RD. Simplified calculation of body-surface area. *N Engl J Med*. 1987;317:1098. https://doi.org/10.1056/NEJM198710223171717.
14. McCarron MM, Devine BJ. Clinical pharmacy: case studies: case number 25 gentamicin therapy. *Drug Intell Clin Pharm*. 1974;8:650–655.
15. Bauer LA. *Applied Clinical Pharmacokinetics*. McGraw-Hill, Medical Publishing Division; 2001.
16. Tessitore N, Mansueto G, Bedogna V, et al. A prospective controlled trial on effect of percutaneous transluminal angioplasty on functioning arteriovenous fistulae survival. *J Am Soc Nephrol*. 2003;14:1623–1627. https://doi.org/10.1097/01.asn.0000069218.31647.39
17. Huijbregts HJ, Bots ML, Wittens CH, et al. Hemodialysis arteriovenous fistula patency revisited: results of a prospective, multicenter initiative. *Clin J Am Soc Nephrol*. 2008;3:714–719. https://doi.org/10.2215/CJN.02950707
18. Perkins NJ, Schisterman EF. The inconsistency of "optimal" cutpoints obtained using two criteria based on the receiver operating characteristic curve. *Am J Epidemiol*. 2006;163:670–675. https://doi.org/10.1093/aje/kwj063
19. Fronek A, Criqui MH, Denenberg J, Langer RD. Common femoral vein dimensions and hemodynamics including valsalva response as a function of sex, age, and ethnicity in a population study. *J Vasc Surg*. 2001;33:1050–1056. https://doi.org/10.1067/mva.2001.113496
20. Hwaung P, Heo M, Bourgeois B, Kennedy S, Shepherd J, Heymsfield SB. Greater height is associated with a larger carotid lumen diameter. *Medicines (Basel)*. 2019;6:57. https://doi.org/10.3390/medicines6020057
21. Krejza J, Arkuszewski M, Kasner SE, et al. Carotid artery diameter in men and women and the relation to body and neck size. *Stroke*. 2006;37:1103–1105. https://doi.org/10.1161/01.STR.0000206440.48756.f7

22. Sandgren T, Sonesson B, Ahlgren R, Länne T. The diameter of the common femoral artery in healthy human: influence of sex, age, and body size. *J Vasc Surg*. 1999;29:503–510. https://doi.org/10.1016/s0741-5214(99)70279-x
23. Hadimeri U, Smedby Ö, Fransson SG, et al. Fistula diameter correlates with echocardiographic characteristics in stable hemodialysis patients. *Nephrology*. 2015;1:E44–E48.
24. Joseph Lo Z, Tay WM, Lee Q, et al. Predictors of radiocephalic arteriovenous fistulae patency in an Asian population. *J Vasc Access*. 2016;17:411–416. https://doi.org/10.5301/jva.5000591
25. Jemcov TK. Morphologic and functional vessels characteristics assessed by ultrasonography for prediction of radiocephalic fistula maturation. *J Vasc Access*. 2013;14:356–363. https://doi.org/10.5301/jva.5000163
26. Miller CD, Robbin ML, Allon M. Gender differences in outcomes of arteriovenous fistulas in hemodialysis patients. *Kidney Int*. 2003;63:346–352. https://doi.org/10.1046/j.1523-1755.2003.00740.x
27. Stehman-Breen CO, Sherrard DJ, Gillen D, Caps M. Determinants of type and timing of initial permanent hemodialysis vascular access. *Kidney Int*. 2000;57:639–645. https://doi.org/10.1046/j.1523-1755.2000.00885.x
28. Hirth RA, Turenne MN, Woods JD, et al. Predictors of type of vascular access in hemodialysis patients. *JAMA*. 1996;276:1303–1308.
29. Kats M, Hawxby AM, Barker J, Allon M. Impact of obesity on arteriovenous fistula outcomes in dialysis patients. *Kidney Int*. 2007;71:39–43.
30. Chan KE, Pflederer TA, Steele DJ, et al. Access survival amongst hemodialysis patients referred for preventive angiography and percutaneous transluminal angioplasty. *Clin J Am Soc Nephrol*. 2011;6:2669–2680. https://doi.org/10.2215/CJN.02860311
31. Paulson WD, Moist L, Lok CE. Vascular access surveillance: an ongoing controversy. *Kidney Int*. 2012;81:132–142. https://doi.org/10.1038/ki.2011.337
32. Polkinghorne KR, Lau KK, Saunder A, Atkins RC, Kerr PG. Does monthly native arteriovenous fistula blood-flow surveillance detect significant stenosis–a randomized controlled trial. *Nephrol Dial Transplant*. 2006;21:2498–2506. https://doi.org/10.1093/ndt/gfl242
33. Bouchouareb D, Saveanu A, Bartoli JM, Olmer M. A new approach to evaluate vascular access in hemodialysis patients. *Artif Organs*. 1998;22:591–595. https://doi.org/10.1046/j.1525-1594.1998.06196.x
34. Monroy-Cuadros M, Salazar A, Yilmaz S, McLaughlin K. Native arteriovenous fistulas: correlation of intra-access blood flow with characteristics of stenoses found during diagnostic angiography. *Semin Dial*. 2008;21:89–92. https://doi.org/10.1111/j.1525-139X.2007.00386.x
35. Tessitore N, Bedogna V, Poli A, et al. Adding access blood flow surveillance to clinical monitoring reduces thrombosis rates and costs, and improves fistula patency in the short term: a controlled cohort study. *Nephrol Dial Transplant*. 2008;23:3578–3584. https://doi.org/10.1093/ndt/gfn275
36. Schwarz C, Mitterbauer C, Boczula M, et al. Flow monitoring: performance characteristics of ultrasound dilution versus color Doppler ultrasound compared with fistulography. *Am J Kidney Dis*. 2003;42:539–545. https://doi.org/10.1016/s0272-6386(03)00786-8
37. Tonelli M, Jindal K, Hirsch D, Taylor S, Kane C, Henbrey S. Screening for subclinical stenosis in native vessel arteriovenous fistulae. *J Am Soc Nephrol*. 2001;12:1729–1733. https://doi.org/10.1681/ASN.V1281729
38. Hoeben H, Abu-Alfa AK, Reilly RF, Aruny JE, Bouman K, Perazella MA. Vascular access surveillance: evaluation of combining dynamic venous pressure and vascular access blood flow measurements. *Am J Nephrol*. 2003;23:403–408. https://doi.org/10.1159/000074297
39. Lok CE, Bhola C, Croxford R, Richardson RM. Reducing vascular access morbidity: a comparative trial of two vascular access monitoring strategies. *Nephrol Dial Transplant*. 2003;18:1174–1180. https://doi.org/10.1093/ndt/gfg122
40. Tonelli M, Hirsch D, Clark TW, et al. Access flow monitoring of patients with native vessel arteriovenous fistulae and previous angioplasty. *J Am Soc Nephrol*. 2002;13:2969–2973. https://doi.org/10.1097/01.asn.0000040597.94103.48