

# Luminal pressure gradient and risk of arteriovenous fistula nonmaturation

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## Abstract

While arteriovenous fistula (AVF) nonmaturation is a major issue of hemodialysis care, an effective treatment to improve AVF maturation remains lacking. AVF introduces pulsatile arterial blood flow into its venous limb and produces high luminal pressure gradient, which may have adverse effect on vascular remodeling. As such, the aim of the present study is to investigate effect of luminal pressure gradient on AVF nonmaturation. This single-center, prospective observational study includes patients receiving autologous AVF creation. Participants received early postoperative ultrasound 5–7 days after surgery to collect parameters including diameters, flow rates, and volume at inflow and outflow sites. Luminal pressure gradient was estimated by using modified Bernoulli equation. The outcome was spontaneous AVF maturation within 8 weeks after surgery without intervention. Thirty patients were included, of which the mean age was 66.9 years and 70% were male. At the end of study, 13 (43.3%) patients had spontaneous AVF maturation. All demographic and laboratory characteristics were similar between patients with mature and nonmature AVF. Regarding ultrasonographic parameters, nonmature AVF showed significantly higher inflow/outflow diameter ratio, inflow velocity, and luminal pressure gradient. While these 3 parameters were significantly correlated, multivariate logistic regression showed their significant association with AVF nonmaturation. Receiver operating characteristic curve exhibited their high predictive value for AVF nonmaturation. Our findings showed that higher inflow/outflow ratio, inflow velocity, and AVF luminal pressure gradient in early postoperative ultrasound predicted risk of AVF nonmaturation. Reducing inflow/outflow diameter ratio or inflow rate may be an approach to improve AVF maturation. The predictive value of this early assessment might have impact on the clinical practice of AVF care.

**Abbreviations:** AUC = area under ROC curve, AVF = arteriovenous fistula, KDOQI = Kidney Dialysis Outcomes and Quality Initiative, ROC curve = receiver operating characteristic curve.

**Keywords:** arteriovenous fistula, end-stage renal disease, hemodialysis, nonmaturation, ultrasound

C-HK and T-IC contributed equally to this work.

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The datasets generated and analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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## 1. Introduction

In Taiwan, the prevalence of patients requiring dialysis had raised from 1448 to 3480 patients per million population during the 2000 to 2017 period.<sup>[1]</sup> Likewise, in USA, the prevalence of end-stage renal disease also increased from 1335 to 2203 patients per million population during that same period.<sup>[2]</sup> As the prevalence of end-stage renal disease has increased enormously, maintaining vascular access for hemodialysis has also become a more important issue. Among various types of hemodialysis vascular access, arteriovenous fistula (AVF) is the recommended one by The Kidney Dialysis Outcomes and Quality Initiative (KDOQI) due to its superior access patency and lower infection rates.<sup>[3-5]</sup> Despite of these advantages, only 30% to 60% of AVF mature to achieve function patency for hemodialysis after its creation.<sup>[6-9]</sup> Such high rates of nonmaturation increases suffering from surgical procedures and adversely affects the medical care of patients on hemodialysis.

A body of research had revealed risk factors of AVF non-maturation, including female gender,<sup>[10-12]</sup> elder age,<sup>[13]</sup> diabetes mellitus.<sup>[10]</sup> Basic research had also proposed molecular mechanisms of AVF nonmaturation, including neointimal hyperplasia, inflammation and oxidative stress caused by surgical procedures, disturbed shear stress, and intramural tensile strain.<sup>[14]</sup> These pathogenic events are suggested to impair outward remodeling of AVF and lead to nonmaturation.<sup>[15-17]</sup> While identifying these risk factors and molecular mechanisms helps us better understand the nature of AVF nonmaturation, a practical and effective strategy to improve AVF maturation is yet to be developed.

With creation of AVF, pulsatile arterial blood flow is introduced, producing non-physiologically high luminal pressure gradient and stretching strain in the venous limb of AVF.<sup>[18]</sup> Such hemodynamic change may modulate genetic expression of venous endothelium, regulate its phenotype and consequently impair the remodeling of AVF.<sup>[19]</sup> This inference is supported by the finding that neointimal hyperplasia mainly occurs at venous limb of AVF, where venous endothelium is exposed to arterial blood flow.<sup>[20]</sup> As such, higher luminal pressure gradient in AVF may impair outward remodeling and maturation, which remained a hypothesis to be confirmed.

Thus, we hypothesized that elevated AVF luminal pressure gradient impairs its maturation. To that end, the aim of this prospective, observational study is to investigate the association between AVF luminal pressure gradient and nonmaturation.

## 2. Materials and Methods

### 2.1. Participants

Patients scheduled to have AVF creation in Wan Fang Hospital from September, 2018 to April, 2019 were assessed for the eligibility of the study. Those who received creation of radio-cephalic, brachio-cephalic, or brachio-basilic AVF, regardless of being at pre-dialysis stage or already on maintenance dialysis treatment, were candidates to be enrolled. The exclusion criteria were as followed: age < 20 years old; impaired cognition or consciousness that prevented the patient to understand the protocol

and to sign informed consent; AVF creation was not feasible due to technical difficulty. Patients eligible for being included were explained on the purpose and the protocol of the study. Those understood the study and agreed to sign the informed consent were included into the study. The present study was approved by the ethics committee and Institutional Review Board of Taipei Medical University (N201801091). All included participants provided informed consent approved by the Institutional Review Board. The entire study was conducted in accordance with the tenets of the 1975 Declaration of Helsinki, as revised in 2000.

### 2.2. Study protocol and outcome definition

Demographic profile and laboratory data were obtained within a week before AVF creation. Participants underwent preoperative ultrasound to define feasibility and optimal site for AVF creation 1 week before AVF creation. A single dose of pre-operative intravenous cephalixin was administered prophylactically. Anticoagulants were avoided from the day of surgery to the 3rd day after surgery. Wound infection, hand ischemia, and AVF bruits were checked on the 1st day after surgery. Between the 5th and the 7th day after surgery, an early postoperative ultrasound was performed to obtain parameters used in the present study (Fig. 1), which will be stated in detail below.

The outcome of the study was spontaneous AVF maturation, which was defined as its successful use for hemodialysis within 8 weeks from its creation without any interventional procedure. Diameters and bruits of AVF were evaluated every clinic visit by attending nephrologists. Once needle puncture was technically feasible based on the decision of the attending nephrologist, AVF puncture was initiated. After 6 consecutive sessions of successful AVF puncture, the AVF was defined as achieving spontaneous maturation. Events that prevented continued AVF puncture included puncture failure, subcutaneous bruising, and insufficient blood flow for hemodialysis sessions. Insufficient blood flow for hemodialysis was defined as failure to provide blood flow 250 mL/min to sustain hemodialysis treatment. In these cases, AVF was withdraw from use and reevaluated by follow-up ultrasound. AVF puncture was performed by a random nurse of the hemodialysis unit of Wan Fang Hospital. Patients with AVF nonmaturation at the end of study were referred to percutaneous transluminal angioplasty for acceleration of AVF maturation or surgical reestablishment of vascular access as appropriate. To avoid selection bias, all patients scheduled to receive AVF were interviewed for participating the study prior to the evaluation of venous mapping. A detailed protocol of the present study had been published elsewhere.<sup>[21]</sup>

### 2.3. Ultrasonographic parameters

The ultrasonography protocol of AVF scanning started with the feeding artery, then artery-to-vein anastomosis, and the outflow venous branches. For radiocephalic fistula, the outflow site was at the proximal cephalic vein 1 cm proximal to the branching point of cephalic vein and median cubital vein.

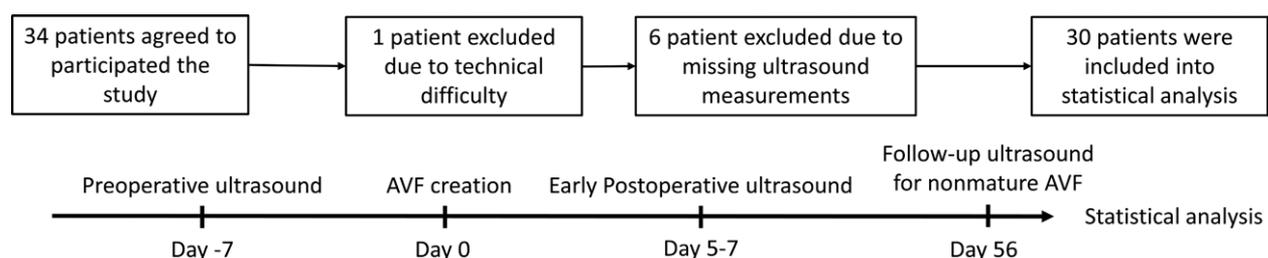


Figure 1. Flow diagram of the study. AVF = arteriovenous fistula.

For brachiocephalic fistula, the outflow site was at the arch vein. For brachobasilic fistula, the outflow site was at axial deep veins. Ultrasonographic parameters were measured at inflow site and outflow site of AVF, which were defined as the artery-to-vein anastomosis and its branches after bifurcation, respectively. Parameters to be obtained included vessel diameter, blood flow volume, and blood flow rate. AVF luminal pressure gradient was estimated by using modified Bernoulli equation as followed: luminal pressure gradient =  $4(\text{inflow rate}^2 - \text{outflow rate}^2)$ . Vascular ultrasound was conducted by using Zonare Ultrasound System, Shenzhen Mindray Bio-Medical Electronics Co. Ultrasound examinations were performed exclusively by 2 regular technicians blinded to the study design to avoid first impression bias.

#### 2.4. Statistical analysis

The study was designed to detect a 100% difference in luminal pressure with 80% power. The post hoc power analysis showed a statistical power of >80%. Continuous variables with normal distribution were expressed as mean  $\pm$  standard deviation, while those deviated from normal distribution were expressed as median (interquartile range). Nominal variables were displayed as frequency and percentage. Statistical tests for continuous variables with normal distribution were conducted by using 2-tailed *t* test for independent samples. For continuous variables deviated from normal distribution, Wilcoxon–Mann–Whitney 2-sample tests were used. Chi-square test or Fisher exact test were used for statistical tests of nominal variables, as appropriate. Correlations between continuous variables were evaluated by using Spearman correlation coefficient. Logistic regression model was used to test the association between candidate predictors and the outcome. Receiver operating characteristic (ROC) curve with Youden criteria was used to determine predictive value and optimal cutoff value for the outcome. Missing data were completely at random and were excluded from the analysis. Statistical significance was defined as a *P* value of <.05. SAS 9.4 (SAS Institute Inc, Cary, NC) was the statistics software used in the present study. Statistical power was calculated by using G power 3.1.9.7.

### 3. Results

#### 3.1. Baseline characteristics of the participants

During the study period, 34 patients who received AVF creation signed informed consents and agreed to participate in the study. Of them, 1 patient was excluded due to technical difficulty in AVF creation and 3 patients were excluded due to missing early postoperative ultrasound measurements. At the end of the study, 30 patients were included into statistical analysis without lost to follow-up (Fig. 1).

Of the included 30 patients, 13 (43.3%) had spontaneous AVF maturation at the end of study. The mean age of participants was 66.9 years and 21 (70%) were of male gender. The mean value of plasma creatinine was 9.1 mg/dL; plasma albumin was 3.5 mg/dL. Of the included AVF, 25 (83.3%) was created at radial artery and 5 (16.7%) were created at brachial artery. Between patients with AVF maturation and nonmaturation, demographic characteristics, including gender, age, presence of diabetes mellitus, coronary artery disease, and cerebrovascular disease were not significantly different. The sites of AVF creation were similar between the 2 groups of patients. Also, patients with AVF maturation and nonmaturation showed no significant difference in the laboratory data obtained, including hemoglobin, blood urea nitrogen, plasma creatinine, Na, K, total calcium, phosphorus, C-reactive protein, and parathyroid hormone. Notably, patients with AVF nonmaturation had lower plasma albumin level, which was not statistically significant ( $3.4 \pm 0.5$  vs  $3.7 \pm 0.5$  mg/dL, *P* = .09). The ratio of first AVF creation was similar between the nonmature and the mature groups (94.1% and 92.3%, respectively, *P* = .84) (Table 1). Remarkably, preoperative ultrasound showed that the diameters of cephalic vein, antecubital vein, brachial vein, and basilic vein were not significantly different between the 2 groups (Table 2).

#### 3.2. Ultrasonographic and hemodynamic characteristics

As stated previously, early postoperative ultrasound was performed between the 5th and the 7th day after surgery. While inflow diameters were similar between patients with AVF maturation and nonmaturation, the diameter of outflow vein was significantly smaller in patients with AVF nonmaturation.

**Table 1**  
Baseline demographic and laboratory characteristics.

Character	Total	Nonmature	Mature	<i>P</i> value
Number, n (%)	30 (100.0)	17 (56.7)	13 (43.3)	n/a
Male, n (%)	21 (70.0)	11 (64.7%)	10 (76.9)	.69
Age, year	66.9 $\pm$ 13.3	68.9 $\pm$ 11.8	64.3 $\pm$ 15.1	.35
DM, n (%)	19 (63.3)	11 (64.7)	8 (61.5)	1.00
CAD, n (%)	4 (13.3)	1 (5.9)	3 (23.1)	.29
CVD, n (%)	3 (10.0)	2 (11.8)	1 (7.7)	1.00
BUN, mg/dL	93.5 $\pm$ 41.1	93.9 $\pm$ 43.9	92.7 $\pm$ 38.0	.94
Cr, mg/dL	9.1 $\pm$ 3.2	8.8 $\pm$ 3.4	9.6 $\pm$ 3.1	.53
Na, mmol/L	135.4 $\pm$ 5.6	136.4 $\pm$ 5.2	133.9 $\pm$ 6.1	.25
K, mmol/L	4.2 $\pm$ 0.6	4.0 $\pm$ 0.4	4.4 $\pm$ 0.8	.16
Ca, mg/dL	8.2 $\pm$ 1.0	8.3 $\pm$ 0.6	8.2 $\pm$ 1.3	.86
P, mg/dL	5.1 $\pm$ 1.7	5.2 $\pm$ 1.3	5.1 $\pm$ 2.1	.96
PTH, pg/mL	215.3 (159.1)	186.0 (155.8)	237.7 (157.4)	.40
Hb, g/dL	9.6 $\pm$ 1.4	9.5 $\pm$ 1.3	9.6 $\pm$ 1.5	.86
Albumin, g/dL	3.5 $\pm$ 0.5	3.4 $\pm$ 0.5	3.7 $\pm$ 0.5	.09
CRP, mg/dL	1.7 (2.4)	2.6 (4.6)	1.3 (1.4)	.89
First AVF, n (%)	28 (93.3)	16 (94.1)	12 (92.3)	.84
AVF site, n (%)				1.00
Radial artery	25 (83.3)	14 (82.4)	11 (84.6)	
Brachial artery	5 (16.7)	3 (17.6)	2 (15.4)	

Continuous variables with normal distribution were expressed as mean  $\pm$  standard deviation. Continuous variables deviated from normal distribution were expressed as median (interquartile range). AVF = arteriovenous fistula, BUN = blood urea nitrogen, CAD = coronary artery disease, Cr = creatinine, CRP = C-reactive protein, CVD = cerebrovascular disease, DM = diabetic mellitus; Hb = hemoglobin, PTH = parathyroid hormone.

**Table 2**  
Preoperative ultrasonographic characteristics.

Diameter, mm	Total	Nonmature	Mature	P value
Cephalic vein	2.9 ± 0.7	2.9 ± 0.8	3.0 ± 0.6	.79
Antecubital vein	4.0 ± 0.8	3.8 ± 0.6	4.4 ± 0.9	.06
Brachial vein	3.6 ± 0.7	3.7 ± 0.7	3.4 ± 0.7	.32
Basilic vein	4.9 ± 1.1	4.6 ± 1.2	5.3 ± 1.0	.10

Continuous variables with normal distribution were expressed as mean ± standard deviation.

Consequently, patients with AVF nonmaturation had significantly higher inflow/outflow diameter ratio. In addition, patients with nonmaturation had significantly higher inflow velocity, while outflow velocities were not significantly different between the 2 groups. Regarding AVF luminal pressure gradient estimated by inflow and outflow velocities, patients with AVF nonmaturation showed significantly higher AVF luminal pressure gradient. Neither inflow volume nor outflow volume were significantly different between patients with AVF maturation and nonmaturation. Brachial systolic pressure and mean arterial pressure were similar between the 2 groups of patients. Nonetheless, brachial diastolic pressure was significantly lower in patients with AVF nonmaturation (Table 3). For the nonmatured AVF, follow-up ultrasound was performed to define the cause of cannulation failure. Among these nonmatured AVFs, the median arterial flow was 389 mL/min; the median AVF flow was 334 mL/min; the mean AVF diameter was 4.3 mm. The cause of cannulation failure was defined as followed: First, AVFs with diameter of <5 mm were defined as failed cannulation due to small AVF caliber. Second, AVFs with diameter of ≥5 mm and blood flow of <500 mL/min were defined as insufficient AVF blood flow. Last, AVFs with diameter of ≥5 mm and blood flow of >500 mL/min but insufficient wall thickness for cannulation were defined as AVF structural weakness. Among the 17 nonmatured AVFs, 5 (29.4%) were attributed to small AVF caliber, 9 (52.9%) were attributed to insufficient AVF blood flow, and 3 (17.7%) were attributed to AVF structural weakness (Table 4).

The correlations between AVF luminal pressure gradient and all other ultrasonographic parameters were evaluated by using Spearman correlation coefficient. Remarkably, AVF luminal pressure gradient showed significant negative correlation with outflow vein diameter and significant positive correlation with inflow/outflow diameter ratio. In addition, higher inflow velocity was significantly positively correlated with AVF luminal pressure gradient. On the other hand, inflow or outflow volume, brachial artery pressures were not significantly correlated with AVF luminal pressure gradient (Table 5). The findings that smaller outflow vein diameter, higher inflow/outflow diameter

ratio, and higher inflow velocity significantly correlated with AVF luminal pressure gradient suggested that both increased inflow/outflow diameter ratio and inflow velocity may increase blood volume in AVF to cause higher AVF luminal pressure gradient.

### 3.3. Ultrasonographic/hemodynamic parameters and risk of AVF nonmaturation

All available ultrasonographic and hemodynamic parameters were evaluated for association with the risk of AVF nonmaturation by using univariable logistic regression and multivariable logistic regression model adjusted by age, gender, and plasma albumin. Only inflow/outflow diameter ratio, inflow velocity, and AVF luminal pressure gradient showed significant association with AVF nonmaturation and significantly associated with risk of AVF nonmaturation in both univariable and multivariable logistic regression models. While outflow vein diameter and brachial diastolic pressure were lower in patients with nonmaturation, these 2 parameters were not significantly associated with AVF nonmaturation in logistic regression models (Table 6).

The 3 ultrasonographic parameters were evaluated for their predictive value for AVF nonmaturation by using ROC curve. The optimal cutoff value for prediction was determined by Youden criteria. Regarding inflow/outflow diameter ratio, the area under ROC curve (AUC) was 0.95 and the optimal cutoff value to predict AVF nonmaturation was >0.92 (Fig. 2A). For inflow velocity, the AUC was 0.91 and the optimal cutoff value to predict AVF nonmaturation was >281 cm/s (Fig. 2B). Finally, AVF luminal pressure gradient showed an AUC of 0.92 and an optimal cutoff value of >29.9 mm Hg on predicting AVF nonmaturation (Fig. 2C). The above findings showed that all these 3 parameters exhibited great prediction value for AVF nonmaturation.

## 4. Discussion

In summary, this prospective observational study showed that among the evaluated ultrasonographic parameters, higher inflow/outflow ratio, inflow velocity, and AVF luminal pressure gradient predicted increased risk of AVF nonmaturation. In addition, the correlation between these 3 parameters inferred that both higher inflow/outflow ratio and higher inflow velocity contributed to increased blood volume in AVF, which subsequently led to elevated AVF luminal pressure gradient to impair AVF maturation.

Flow and pressure surveillance has been recommended by KDOQI guidelines to detect AVF stenosis.<sup>[22]</sup> Taken for example, previous studies had shown that AVF flow volume of <400–500 mL/min<sup>[23,24]</sup> and a ratio of intra-access pressure to mean

**Table 3**  
Early postoperative ultrasonographic characteristics.

Character	Total	Nonmature	Mature	P value
Inflow diameter, mm	4.4 ± 0.9	4.3 ± 0.8	4.7 ± 0.9	.21
Outflow diameter, mm	4.9 ± 1.4	3.9 ± 0.6	6.2 ± 1.1	<.01
Inflow/outflow diameter ratio	1.0 ± 0.3	1.1 ± 0.2	0.8 ± 0.1	<.01
Inflow volume, mL/min	729.3 (559.3)	681.3 (442.1)	852.7 (991.4)	.78
Outflow volume, mL/min	127.5 (220.8)	194.1 (188.4)	126.0 (244.1)	.53
Inflow velocity, cm/s	249.5 (144)	328 (87)	186 (77)	<.01
Outflow velocity, cm/s	48.5 (48.4)	52.2 (36.8)	39.0 (62.5)	.77
Luminal pressure gradient, mm Hg	24.5 (31.1)	41.6 (19.4)	10.6 (12.5)	<.01
SBP, mm Hg	135.8 ± 22.5	132.8 ± 25.5	141.8 ± 14.8	.44
DBP, mm Hg	73.4 ± 11.0	69.8 ± 10.4	80.7 ± 9.1	.05
MAP, mm Hg	115.0 ± 17.9	111.8 ± 19.9	121.4 ± 11.8	.30

Continuous variables with normal distribution were expressed as mean ± standard deviation. Continuous variables deviated from normal distribution were expressed as median (interquartile range). DBP = diastolic brachial blood pressure, MAP = mean arterial pressure, SBP = systolic brachial blood pressure.

**Table 4**  
**Characteristics of nonmatured AVF.**

Follow-up vascular ultrasound	
Arterial blood flow, mL/min	389 (443)
AVF blood flow, mL/min	334 (465)
AVF diameter, mm	4.3 ± 0.9
Caused of cannulation failure, n (%)	
Small AVF caliber	5 (29.4)
Insufficient AVF blood flow	9 (52.9)
AVF structural weakness	3 (17.7)

Continuous variables with normal distribution were expressed as mean ± standard deviation. Continuous variables deviated from normal distribution were expressed as median (interquartile range). AVF = arteriovenous fistula.

arterial pressure of > 0.55<sup>[25]</sup> suggest outflow stenosis of vascular access. Nonetheless, while these parameters detect stenotic lesions that already exist, whether flow or pressure parameters really predict AVF nonmaturation or lesions to be formed remain unknown. In an animal study documenting changes in diameter, flow, and pressure drop in porcine AVF from postoperative day 2 to 28, Rajabi-Jagahrgh et al provided clues to this question. In this work, they showed that pressure drop in AVF was positively correlated with inflow velocity. In addition, AVF with adverse remodeling exhibited higher pressure drop than those with favorable remodeling (20.9 vs 6.6 mm Hg).<sup>[26]</sup> This previous study supports our findings that inflow velocity positively correlated with AVF luminal pressure gradient and that higher post-operational AVF luminal pressure gradient was associated increased risk of AVF nonmaturation.

Contemporarily, AVF nonmaturation has been attributed to the theory of inward/outward remodeling imbalance, which suggests that impaired vasodilation (outward remodeling)<sup>[16,27]</sup> and intimal hyperplasia (inward remodeling)<sup>[28,29]</sup> act collectively to cause AVF nonmaturation.<sup>[17]</sup> While impaired vasodilation is related to underlying cardiovascular diseases, the pathogenesis that causes AVF intimal hyperplasia remains an issue of debate. In a prospective, observational study, Allon et al showed that in nonmatured AVF, intimal hyperplasia did not preexist at baseline but developed de novo after AVF creation.<sup>[30]</sup> Taken together with these previous studies, increased luminal pressure gradient that developed after AVF creation may be one of the causes that lead to intimal hyperplasia and nonmaturation.

Currently, KDOQI guidelines recommend no specific surgical or endovascular maneuvers to facilitate AVF maturation. Neither do they recommend a minimum diameter threshold to create an AVF.<sup>[5]</sup> While several studies had suggested a minimum vein diameter of > 2.0–2.5 mm for radiocephalic AVF

**Table 5**  
**Correlations between AVF luminal pressure gradient and early postoperative ultrasonographic/hemodynamic parameters\*.**

Character	Correlation coefficient	P value
Inflow diameter	-0.17	.38
Outflow diameter	-0.65	<.01
Inflow/outflow diameter ratio	0.61	<.01
Inflow volume	0.04	.85
Outflow volume	0.04	.85
Inflow velocity	0.97	<.01
Outflow velocity	0.02	.91
SBP	0.10	.68
DBP	-0.31	.20
MAP	0.01	.96

\*By Spearman correlation coefficient.

AVF = arteriovenous fistula, DBP = diastolic brachial blood pressure, MAP = mean arterial pressure, SBP = systolic brachial blood pressure.

and > 3–3.4 mm for brachiocephalic/brachiobasilic AVF,<sup>[31–33]</sup> surgical recommendations for AVF creation other than vein diameter at anastomosis remain lacking. Nonetheless, the results of the present study may provide some clues on this issue. Our results showed that higher inflow/outflow diameter ratio, inflow velocity, and luminal pressure gradient were associated higher risk of AVF nonmaturation. As a result, pre-operative evaluation for surgical planning to reduce inflow/outflow diameter ratio or inflow velocity may limit luminal pressure gradient, which in turn improves AVF maturation. However, this approach needs to be investigated in a prospective, interventional trial.

A limitation of the present study was small number of participants and low statistic power, which may obscure the effect of less influential predictors for AVF nonmaturation. In addition, AVF luminal pressure gradient was not a directly measured value. Thus, the precision of this evaluated value should be carefully considered in interpretation. Then, the single-center design restricted the extension of our findings to the entire hemodialysis population. A last limitation would be the effects of unmeasured confounding factors that were not considered in the multivariable analysis. On the other hand, the strength of the present study included prospective design that allowed complete data collection, standardized ultrasound technique that allowed consistent measurements. Lastly, the approach of this study required only Doppler ultrasound, which made it applicable in most district hospitals.

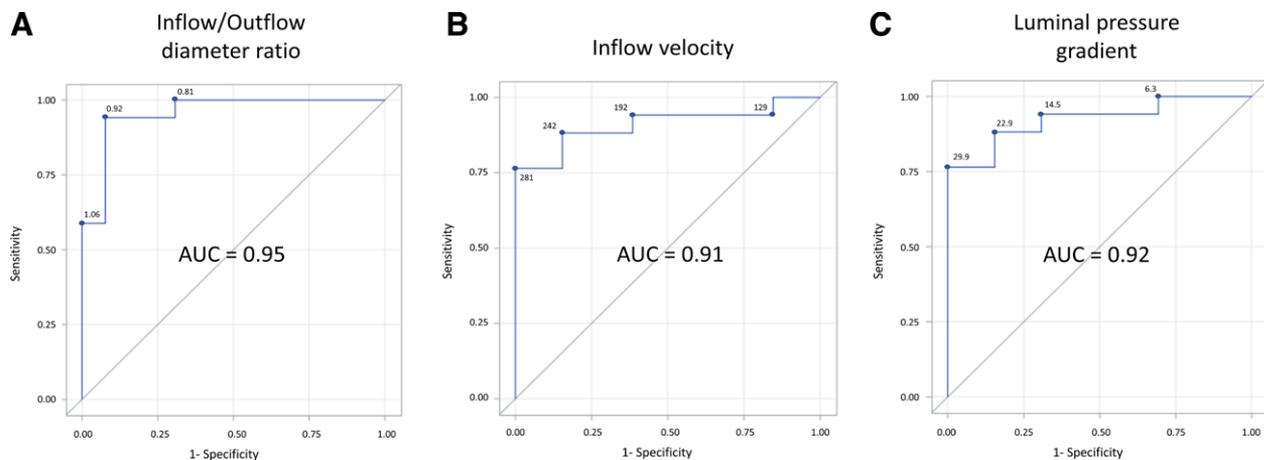
In conclusion, this study showed that in an early postoperative vascular ultrasound examination (5–7 day after

**Table 6**  
**Early postoperative ultrasonographic/hemodynamic parameters and risk for AVF nonmaturation.**

Character	Univariate		Multivariate*	
	OR (95% CI)	P value	OR (95% CI)	P value
Inflow diameter per 0.1 mm increment	0.9 (0.8–1.0)	.21	1.0 (0.9–1.1)	.51
Outflow diameter per 0.1 mm increment	0.5 (0.2–1.1)	.08	0.1 (0.1–14.5)	.34
Inflow/outflow diameter ratio per 0.01 increment	1.2 (1.1–1.4)	<.01	1.4 (0.9–1.9)	.05
Inflow volume per 10 mL/min increment	1.0 (0.9–1.0)	.21	1.0 (0.9–1.0)	.63
Outflow volume per 10 mL/min increment	1.0 (0.9–1.0)	.96	1.0 (0.9–1.0)	.43
Inflow velocity per 10 cm/s increment	1.3 (1.1–1.6)	<.01	1.3 (1.1–1.6)	.02
Outflow velocity per 10 cm/s increment	1.0 (0.9–1.1)	.95	1.0 (0.9–1.2)	.60
SBP per 10 mm Hg increment	0.8 (0.5–1.3)	.42	0.8 (0.5–1.3)	.40
DBP per 10 mm Hg increment	0.3 (0.1–1.1)	.07	0.3 (0.1–1.3)	.11
Luminal pressure gradient per 10 mm Hg increment	4.8 (1.6–14.3)	<.01	4.9 (1.5–16.3)	.01

\*Model adjusted by age, gender, and plasma albumin.

AVF = arteriovenous fistula, DBP = diastolic brachial blood pressure, SBP = systolic brachial blood pressure.



**Figure 2.** ROC curve demonstrating the predictive value of ultrasonographic parameters for AVF nonmaturation. A larger AUC suggests higher predictivity of the indexed predictor. The point with minimal distance to the upper left corner on the curve is the best discriminative value. (A) Inflow/Outflow diameter ratio, cutoff value:  $>0.92$ ; (B) Inflow velocity, cutoff value:  $>281$  cm/s; (C) AVF Luminal pressure gradient, cutoff value:  $>29.9$  mm Hg. The models were constructed by using univariable logistic regression and the optimal cutoff value were determined by Youden criteria. AUC = area under ROC curve, AVF = arteriovenous fistula, ROC curve = receiver operating characteristic curve.

surgery), higher inflow/outflow ratio, inflow velocity, and AVF luminal pressure gradient predicted increased risk of AVF nonmaturation. The predictive value of this early assessment might have impact on the clinical practice of AVF care. In future, surgical planning to reduce inflow/outflow diameter ratio or inflow rate may be an approach to reduce luminal pressure gradient, which may consequently improve AVF maturation.

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