One-year patency rate of native arteriovenous fistulas reconstructed by vascular stripping in hemodialysis patients with venous neointimal hyperplasia

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Objective: **There are limited therapeutic measures for stenosis of arteriovenous fistulas (AVFs) due to venous neointimal hyperplasia (VNH). In the current retrospective study, we reviewed the clinical data of hemodialysis patients who underwent AVF reconstruction by VNH stripping. The primary measure of interest was the secondary patency rate of the restored AVF.**

Methods: **The study included hemodialysis patients who underwent AVF reconstruction by VNH stripping (group A), AVF reconstruction proximal to the original fistula (group B), or creation of a new AVF (group C). Patency was evaluated immediately after the surgery and at follow-up visits.**

Results: **Of 353 patients who underwent AVF reconstructions, 327 (91.9%) were for late AVF failure. The final analysis included 305 patients: 76, 128, and 101 patients in groups A, B, and C, respectively. The three groups were comparable in age, sex, causes for AVF, AVF sites, and the artery for the AVF ($P > .05$). At 3-month follow-up, the secondary AVF patency rate was comparable across the three groups at 93.4%, 92.2%, and 92.1% in groups A, B, and C, respectively. The patency rate at 6 and 12 months was also comparable across groups A, B, and C at 89.5%, 89.8%, and 88.1% at 6 months and 84.2%, 85.9%, and 81.2% at 12 months, respectively.**

Conclusions: **Reconstructing the AVF by surgically removing VNH is an effective technique for late hemodialysis access failure, with maximal preservation of blood vessels. (J Vasc Surg 2015;61:192-6.)**

A native arteriovenous (AV) fistula (AVF) is the preferred choice for permanent hemodialysis because of the low incidence of infection and thrombosis and high long-term patency.[1] However, a mature AVF may still develop venous neointimal hyperplasia (VNH) after a period of successful use, leading to venous stenosis with or without thrombosis. Failure of an AVF vascular access can be early (failed maturation of AV anastomosis, typically in <3 months after AVF creation) or late (>3 months after AVF creation).[2] The most important factor causing late failure is venous stenosis, particularly perianastomotic stricture due to VNH formation.

In most patients, VNH is managed with percutaneous transluminal angioplasty (PTA). However, PTA itself can induce vascular injury, myofibroblast migration and proliferation, and abnormal vascular remodeling, and consequently, relapsed AVF stricture.[3,4] A new AV anastomosis proximal to a previous fistula or the use of blood vessels from a different location are option, but at the cost of a part of the vasculature.

We recently developed an operative technique to repair AVFs by surgical stripping of VNH and AV reanastomosis.[5] In the current retrospective study, we reviewed the clinical data of hemodialysis patients who had undergone AVF reconstruction by VNH stripping. The primary interest of the analysis was the secondary patency rate of restored AVF.

METHODS

The Institutional Review Board of First Hospital of Tsinghua University, Beijing, China, approved the study protocol.

Patients. The current study included all hemodialysis patients who underwent AVF reconstruction by VNH stripping between January 2007 and December 2011 at the First Hospital of Tsinghua University. The criteria for inclusion in the analysis were forearm or upper arm AVF access with the anastomosis performed below the elbow and late (>3 months after AVF establishment) AVF failure or dysfunction (hemodialysis blood flow of <200 mL/min). The analysis excluded patients with early AVF access failure or dysfunction (<3 months after AVF establishment), upper arm (anastomosis created above the elbow) AVF, AVF grafts, or death or loss to follow-up. Patient consent was not required because of the retrospective nature of this study.

The surgical technique. All patients provided written informed consent for the treatment before surgery. The

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Author conflict of interest: none.

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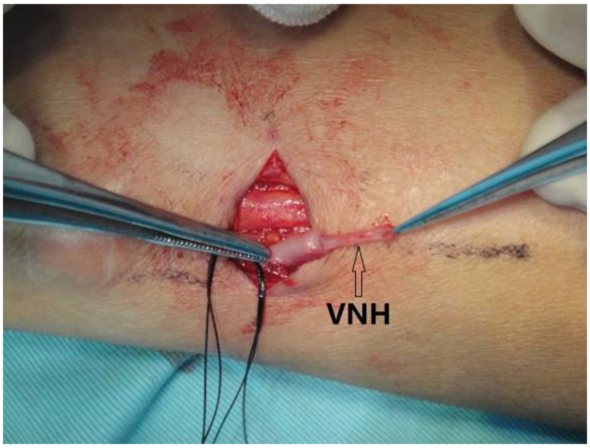


Fig 1. Stripping of venous neointimal hyperplasia (*VNH*) is done with forceps down-folding the normal surrounding vascular wall like "taking off socks."

protocols included AVF reconstruction by VNH stripping (group A), AVF reconstruction proximal to the original fistula (group B), and creation of a new AVF (group C). Selection of the protocol was based on physician discretion. Major indications for AVF reconstruction by VNH stripping were:

1. Paraanastomotic VNH or venous stenosis, or both, in an AVF at any location in the forearm, including a radial-cephalic or ulnar-basilic fistula;
2. Sufficient vein for cannulation in the forearm and upper arm;
3. Blood flow during hemodialysis at <200 mL/min in the absence of thrombus or <300 mL/min if patients required high-flux dialysis or hemodiafiltration therapy while other interventions were unsuccessful;
4. ≤7 days after complete fistula occlusion by thrombus.

Contraindications were proximal venous (including the central vein) or arterial stenosis, or both, in the forearm.

The same surgeon performed all three types of operation. The AVF was established in an end-to-side pattern. A newly created or reconstructed AVF proximal to the previous fistula, with or without resection of the occluded vein, was made according to the standard protocols for fistula construction.[6] VNH stripping was performed as previously described.[5] Briefly, patients were placed supine or sitting with the operated-on arm laterally rotated and abducted. Blood vessels were marked using a Sharpie pen (Newell Rubbermaid, Downers Grove, Ill), or methyl violet.

After disinfection and local anesthesia with 1% lidocaine, a transverse incision was made proximal to the original anastomosis and a preferable 3-cm segment of the venous end (cephalic or basilic) was dissected for reaching and reanastomosis with the artery. Venous thrombus, if present, was removed, and t6he vein was flushed using a 10-mL syringe connected to a noninvasive needle and by injecting 20 to 50 mL heparinized saline into the vascular lumen. VNH was then carefully stripped with forceps, down-folding the normal surrounding vascular wall like "taking off socks" (Fig 1). The artery was dissected, and finally, an end-to-side AV anastomosis was made using a 7-0 vascular suture.

Follow-up study. AVF patency was evaluated immediately, 1 day, and 2 weeks after the procedure. Follow-up was performed at 3-month intervals until 12 months. The examination included palpating of the thrill, auscultation of the bruit, and assessment of hemodialysis outcome.

Patency was defined as (1) the presence of fistulous vascular pulsation and palpable thrill, (2) the presence of audible continuous vascular murmurs, (3) ≥200 mL/min blood flow rate needed for hemodialysis, and (4) no intervention required to maintain patency. Primary patency was defined as intervention-free access survival from the time of surgical creation to the first access thrombosis or access salvage procedure aimed at maintaining or re-establishing patency or to the time of measurement of patency.[2] Secondary patency was defined as the interval from AVF reconstruction or surgical creation of a new AVF until access abandonment or the time patency was measured.

Primary failure was defined as an AVF that did not develop to maintain dialysis or became thrombosed before the first successful cannulation for hemodialysis treatment. Secondary failure was defined as permanent failure of the AVF after it had achieved adequacy for hemodialysis. The primary outcome of this retrospective study was secondary patency rates.

Statistical analysis. Data are expressed as mean ± standard deviation and were analyzed by the Student *t*-test using SPSS 10.0 software (SPSS Inc, Chicago, Ill). Enumeration data were analyzed by χ^2 test. Patency rate was analyzed using the Kaplan-Meier method. Data from patients who died or underwent renal transplantation during the study period were censored. Statistical significance was set at $P < .05$.

RESULTS

Patient demographic and baseline characteristics. The study flowchart is shown in Fig 2. Late AVF failure occurred in 327 of the 353 patients (91.9%) who underwent an AVF operation. AVF reconstruction was by VNH stripping (group A) in 76 patients (23.2%), was proximal to the original fistula (group B) in 128 (39.1%), and a new AVF (group C) was created in 101 (30.9%). Four patients in group A were excluded due to death (n = 3) or loss to follow-up (n = 1), 10 patients in group B were excluded due to death (n = 4) or loss to follow-up (n = 6), and eight patients in group C were excluded due to death (n = 3) or loss to follow-up (n = 5). Consequently, 305 patients were included in the final analysis: 76 in group A, 128 in group B, and 101 in group C.

The patient demographic and baseline characteristics are listed in Table I. Patients were a mean age of 57.7 ± 15.7 years (range, 20-86 years), and there were slightly

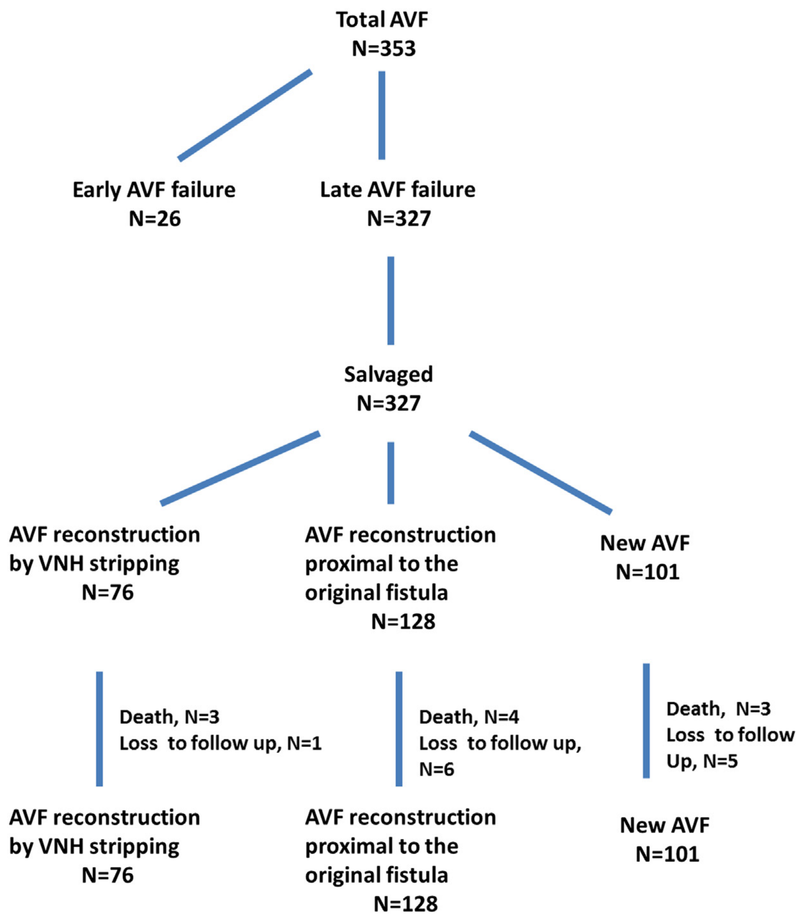


Fig 2. Flowchart of patients in the study. *AVF,* Arteriovenous fistula; *VNH,* venous neointimal hyperplasia.

more women (52.1%) than men (47.9%). Hemodialysis was required because of diabetic nephropathy in 35.1% of patients, chronic glomerulonephritis in 27.9%, and hypertensive nephropathy in 26.6%. Most AVF sites were in the left forearm (70.8%), followed by AVFs in the right forearm (25.9%). Most AVFs used the radial artery (93.4%). The differences in age, sex, causes for AVF, AVF sites, and the artery used for AVF among the three groups were not statistically significant ($P > .05$; Table II).

Secondary patency rates. The Kaplan-Meier curve of patency rates is shown in Fig 3. Most patients (93.4%) who had undergone AVF reconstruction by VNH stripping maintained AVF patency at 3 months of follow-up, with the patency rate comparable to, though slightly higher than, that of patients who had undergone AVF reconstruction proximal to the original fistula (92.2%) and of patients with a new AVF (92.1%; $P > .05$). The patency rate of AVFs treated with VNH stripping declined to 89.5% at 6 months and to 84.2% at 1 year after AVF reconstruction. Similar declines were observed in patency rates of AVFs proximal to the original fistula (6 months: 89.8%; 12 months: 85.9%) and new AVFs (6 months: 88.1%; 12 months: 81.2%). The patency rates at 6 months and 1 year after salvage remained comparable among the three groups ($P > .05$).

DISCUSSION

As an effective and safe vascular access, the AVF has been applied in hemodialysis patients for nearly 50 years. The notion of "autologous AV fistula first" has been proposed by the United States 2006 National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI) Clinical Practice Guidelines for Vascular Access. However, with extended survival of hemodialysis patients and an increasing trend in the morbidities of diabetes, hypertension, and obesity, establishment of AVFs becomes increasingly difficult, and AVF-associated complications have also been on the rise. An increase in hospitalization and treatment costs resulting from fistula failure has been a great concern for dialysis patients. The development of venous stenosis likely involves uremia itself, operative technique, and hemodynamic and pathophysiologic factors.[7,8]

Major therapeutic approaches for VNH-caused fistulous vascular stricture include (1) PTA and endovascular

Table I. Patient demographic and baseline characteristics

Variables	*All patients*	*Group A*	*Group B*	*Group C*
AVF, No. (%)	305 (100)	76 (24.9)	128 (42.0)	101 (33.1)
Age, years				
Mean ± SD	57.7 ± 15.7	59.7 ± 12.7	58 ± 16.1	55.8 ± 17.1
Range	20-86	20-83	22-83	20-86
Male, No. (%)	146 (47.9)	39 (51.3)	61 (47.7)	46 (45.6)
Need for AVF, No. (%)				
Chronic glomerulonephritis	85 (27.9)	21 (27.6)	31 (24.2)	33 (32.7)
Diabetic nephropathy	107 (35.1)	29 (38.2)	50 (39.1)	28 (27.7)
Hypertensive nephropathy	81 (26.6)	19 (25.0)	36 (28.1)	26 (25.7)
Drug toxicities	17 (5.6)	3 (3.9)	6 (4.7)	8 (7.9)
Polycystic kidneys	7 (2.3)	2 (2.6)	2 (1.6)	3 (3.0)
Unknown	7 (2.3)	2 (2.6)	3 (2.3)	2 (2.0)
AVF sites, No. (%)				
Left forearm	216 (70.8)	54 (71.1)	89 (69.5)	73 (72.3)
Right forearm	79 (25.9)	22 (28.9)	30 (23.4)	27 (26.7)
Right upper arm	4 (1.3)	0 (0.0)	4 (3.1)	0 (0.0)
Left upper arm	6 (2.0)	0 (0.0)	5 (3.9)	1 (1.0)
AVF artery, No. (%)				
Radial	285 (93.4)	70 (92.1)	121 (94.5)	94 (93.1)
Ulnar	20 (6.6)	6 (7.9)	7 (5.5)	7 (6.9)

AVF, Arteriovenous fistula; *Group A,* AVF reconstruction by venous neointimal hyperplasia (VNH) stripping; *Group B,* AVF reconstruction proximal to the original fistula; *Group C,* newly created AVF; *SD,* standard deviation.

Table II. Patency rates of arteriovenous fistulas (*AVFs*)

Variables	*Group A, No. (%)*	*Group B, No. (%)*	*Group C, No. (%)*	χ^2	P
Immediately after surgery	76 (100)	128 (100)	101 (100)		
Follow-up					
2 weeks	76 (100)	128 (100)	101 (100)		
3 months	71 (93.4)	118 (92.2)	93 (92.1)	0.125	.935
6 months	68 (89.5)	115 (89.8)	89 (88.1)	0.183	.913
12 months	64 (84.2)	110 (85.9)	82 (81.2)	0.095	.622

Group A, AVF reconstruction by venous neointimal hyperplasia (VNH) stripping; *Group B,* AVF reconstruction proximal to the original fistula; *Group C,* newly created AVF.

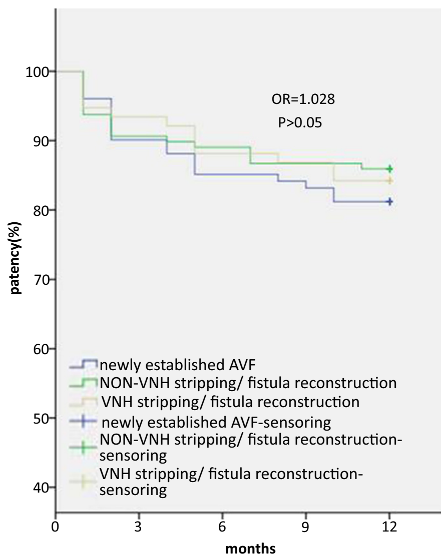
stenting,[3] (2) endovascular thrombectomy by a Fogarty catheter, (3) AV reanastomosis proximal to the narrowed site, and (4) vascular grafts. Among these techniques, PTA is the primary choice recommended in the NKF-K/DOQI guidelines.

Gmelin et al[9] first introduced PTA to treat fistula stenosis in 1989. Its advantages include safety and efficacy, less vascular injury, easy surgical operation, and repeatable fistulous vasodilation at multiple time and locations. In addition, this procedure is carried out in the original fistula vessels and does not waste additional native blood vessels, shortens the time of fistula maturation, and has fewer complications.[3] Yet, one of the disadvantages using PTA is the likelihood of AVF stricture relapse. Tessitore et al[10] reported that the incidence of relapsed stricture after PTA was markedly higher than after surgical fistula reconstruction ($P = .009$). Napoli et al[11] also demonstrated that surgical treatment for narrow or occluded fistulas resulted in better initial patency than other approaches.

In contrast to the traditional surgical procedure, which usually abandons part of the fistulous vessels, we treated 76 hemodialysis patients with late AVF failure by surgical stripping of VNH and successfully preserved the original fistulous vessels. This operation to restore the AVF achieves a fistula patency rate comparable to that resulting from the initially created AVF or an AVF reconstructed proximally to the original fistula, with or without resection of occluded vein. Thus, this offers an effective alternative treatment choice for patients with AVF when PTA or PTA plus stenting are not readily available, such as in most community hospitals in developing countries.

The restored AVF by VNH stripping can be used for hemodialysis immediately after the operation, and waiting for several weeks for fistula maturation is not necessary because the veins have already arterialized. A little residual VNH may remain with the procedure but will not affect the venous lumen and will recover by itself after restoration of blood flow.

The mechanism by which the fistulous vascular lumen repairs itself after VNH stripping is unclear, presumably by endothelial remodeling or re-endothelialization with the restoration of lumen patency. Pathologic examination of VNH specimens reveals that there still are endothelial gaps filled with CD34 and factor VIII-positive cells between the vascular wall and the VNH tissue (data not presented), indicating that residual endothelial cells may



	0	3	6	9	12
newly established AVF	101	91	86	84	82
NON-VNH stripping/ fistula reconstruction	128	116	114	111	110
VNH stripping/ fistula reconstruction	76	71	67	66	64

Fig 3. The Kaplan-Meier curve of patency rates. The numbers at the bottom represent the number of patients at risk for each interval. *AVF,* Arteriovenous fistula; *OR,* odds ratio; *VNH,* venous neointimal hyperplasia.

participate in the re-endothelialization process of venous lumen after stripping of VNH. Amelioration of uremia by hemodialysis significantly increases the number of circulating endothelial progenitor cells and improves endothelial function in end-stage nephropathy.[12,13] Thus, restarting dialysis therapy as quickly as possible may also be beneficial for the reconstructed AVF to be functional and to restore fistula patency.

CONCLUSIONS

We have demonstrated long-term patency rates of AVFs reconstructed by surgically removing VNH and reanastomosis that are comparable with the patency rates obtained by other surgical approaches. This procedure provides maximal preservation of blood vessels for long-term hemodialysis, shortens the time to restart hemodialysis therapy using the fistula, and can be a substitutive operation for failed AVFs.

AUTHOR CONTRIBUTIONS

Conception and design: FL
Analysis and interpretation: FL
Data collection: FL, LL, ZL
Writing the article: FL, LL
Critical revision of the article: FL
Final approval of the article: FL, LL, ZL
Statistical analysis: LL
Obtained funding: Not applicable
Overall responsibility: FL

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