J Am Soc Nephrol 9: 1507–1510, 1998

Subclavian Vascular Access Stenosis in Dialysis Patients: Natural History and Risk Factors

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Abstract. Stenosis of the subclavian vein (SVS) after cannulation occurs in 15 to 50% of chronic hemodialysis patients, and impedes the placement of an arteriovenous fistula in the ipsilateral arm. Its natural history and pathogenic mechanisms are not well established. This study examined 42 consecutive chronic renal failure patients (28 men and 14 women; 46 ± 19 yr) in whom subclavian catheters had been placed as the initial vascular access for hemodialysis. All patients underwent sequential venography studies: at baseline (24 to 48 h after removal of the catheter) and 1, 3, and 6 mo thereafter. Venograms were considered abnormal when there was evidence of unequivocal strictures (more than 30% narrowing), with or without collateral circulation. At baseline, 52.4% (n = 22) of patients showed stenotic vein lesions (n = 19) or total thrombosis (n = 3), and identical lesions were also observed after 1 mo. Surprisingly, 10 of 22 patients with initial SVS (45.4%) showed spontaneous recanalization of venous lesions in the venographies performed 3 mo after removal. The patients with normal baseline venograms (n = 20) showed no change during follow-up. Patients with definitive stenosis at 6 mo (n = 12) had a higher number of inserted catheters (1.58 ± 0.6 *versus* 1.2 ± 0.48; $P < 0.05$), longer time in place (49.08 ± 32.2 *versus* 29.03 ± 26.6 d; $P < 0.05$), and higher number of dialysis sessions (21 ± 13.8 *versus* 12.4 ± 11.4; $P < 0.05$) than those without SVS or with spontaneous recanalization of venous lesions during follow-up. Furthermore, a higher number of catheter-related infections were observed in patients with definitive SVS (66.6% *versus* 33.3%; $P < 0.05$). In summary, SVS is observed in more than half of patients 24 to 48 h after catheter removal and 1 mo later. Even when recanalization occurs in many cases, a definitive stenosis is seen in 28% of patients by the third month. Thus, the creation of an ipsilateral vascular access is possible provided that venography is normal at this time. Finally, mechanical factors and catheter-related infections are the major risk factors for the development of late SVS.

After two decades, subclavian vein cannulation has become a well established route for vascular access in hemodialysis patients (1,2). Nevertheless, the incidence of subclavian vein stenosis (SVS) ranges between 15 and 50%, when the vascular tree is systematically studied using radiologic methods (3–12). In many patients, SVS does not allow the placement of an arteriovenous fistula in the ipsilateral arm. This is clearly of great concern, and SVS must be identified before performing a permanent vascular access. However, little is known about the natural history of SVS, and the optimal time period after catheter removal to perform a venography in order to rule out SVS is not well established.

The pathogenic mechanisms causing this complication are not well understood, although several hypotheses have been suggested (7,8). We have recently identified catheter-related infections as an additional factor associated with SVS (12). The present prospective study was undertaken to investigate the natural history of SVS and to identify risk factors for the development of this complication.

Received July 10, 1997. Accepted November 20, 1997.

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1046-6673/0908-1507$03.00/0
Journal of the American Society of Nephrology

Materials and Methods

Patients

From October 1992 to November 1995, we studied 42 consecutive chronic renal failure patients whose subclavian vein was cannulated for the first time as a vascular access for hemodialysis. All catheters were single-lumen, 20 cm long, and 8F (Vas-Cath, Inc., Mississauga, Ontario, Canada), except in eight instances in which double-lumen catheters were used (Mahurkar catheter 11.5 Fr, Quinton, Seattle, WA). All of the catheters were made of polyurethane. Five experienced staff nephrologists inserted the catheters under stringent aseptic conditions. Catheters were inserted percutaneously using a suitable needle and cannula and the catheter-over-wire technique (13). The placements were atraumatic, and no acute complications were observed during the study. No subcutaneous tunnel was made. Chest radiography with forced exhalation was performed to verify the correct placement of catheters. After successful catheterization, sterile occlusive dressing was used. No antibiotic ointment was applied to the exit site. Catheters were fixed to the skin by means of a single suture and were covered by gauzes impregnated in 10% iodine-povidone that were changed after each dialysis session. Catheter patency was accomplished by instillation of 1.5 cc of sodium heparin (1000 UI/cc) solution every 12 h. The same volume was flushed in each lumen of double lumen catheters. All of the catheters were used exclusively for hemodialysis.

In cases of inadequate blood flow for dialysis or clotting, the catheters were replaced using a sterile guide-wire through the original catheter. This was performed in 10 patients, and always under strict aseptic conditions.

Catheters were withdrawn when the definitive vascular access functioned properly or when a catheter-related infection was suspected. The diagnosis of infection was established in the presence of: (*1*) isolated fever associated with colonization of the catheter tip (<15 colony-forming units), with negative blood cultures and no other apparent source of infection, which disappeared after catheter removal (n = 7; *Staphylococcus epidermidis* in all cases); (*2*) catheter-related sepsis: catheter infection with the same organism found in blood culture and associated clinical signs of sepsis (n = 6; two *Staphylococcus epidermidis,* two *Pseudomona aeruginosa*, one *Klebsiella pneumoniae*, one *Staphylococcus aureus*); (*3*) catheter-related sepsis and ipsilateral phlebitis (n = 1; *Staphylococcus aureus*); and (*4*) exit-site infection: discharge at skin exit site with positive culture (n = 4; three *Staphylococcus epidermidis*, one *Pseudomona aeruginosa*) (12). After removal of all catheters, the distal 5 cm of the catheter was always cultured by the Maki semiquantitative technique (14).

Venographic Studies

All patients underwent sequential venography studies as follows: at baseline (24 to 48 h after catheter removal) and 1, 3, and 6 mo thereafter. Seventy percent of venography studies were performed by conventional radiologic means. Forty cc of iohexol water-soluble contrast (Omnitrast 350) were administered through an elbow at an infusion rate of 4 ml/s. Films were taken at 1-s intervals for 5 s with the patient breathing in deeply. The rest of the venography studies (30%) were performed using digital subtraction (Philips, Integris 3000) by injecting 30 cc of contrast media at the same infusion rate and obtaining images in the venous return phase (1 frame per second during 5 s).

Results were evaluated by a single observer (Dr. Díaz), who did not know the clinical details. The venograms were considered abnormal when there was evidence of unequivocal strictures (more than 30% narrowing of the vessel lumen diameter), with or without collateral circulation (7,8,12). Minor vessel-wall changes without stenosis were not considered abnormal. No patient received antiplatelet or anticoagulant therapy.

Statistical Analyses

Unpaired *t* test, Mann-Whitney *U* analysis, and Fisher exact test were used as appropriate. Data are expressed as mean ± SD, and a P value <0.05 was considered significant. Statistical analyses were performed using the Rsigma® package (Horus Hardware, Madrid, Spain).

Results

No patient had immediate complications at the time of catheter placement. Figure 1 shows the results of our sequential venography study. At baseline, 52.4% (n = 22) of patients showed stenotic vein lesions (n = 19) or total thrombosis (n = 3), and identical lesions were observed 1 mo later. However, 10 of the 22 patients with SVS (45.4%) surprisingly showed recanalization of venous lesions in the venograms performed 3 mo after catheter removal. Those patients with a normal baseline venography (n = 20) showed no changes during follow-up.

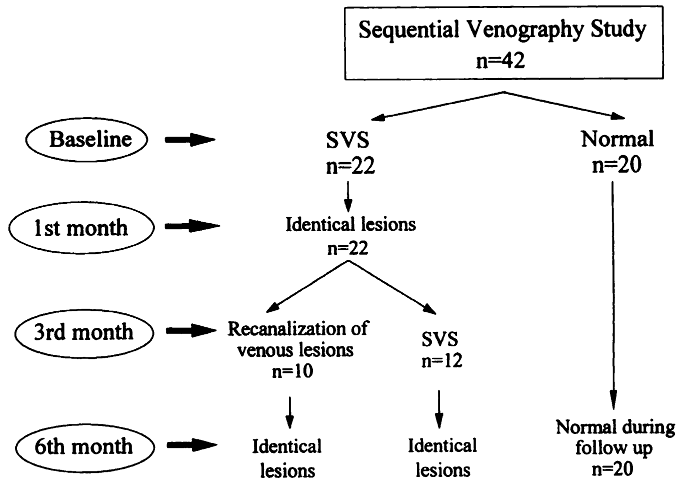

Figure 1. Sequential venographic studies undertaken in 42 consecutive hemodialysis patients subjected to subclavian vein cannulation.

Table 1 shows the clinical characteristics of the patients with or without SVS at baseline. The number of catheters inserted per patient, time of catheter in place, and the number of dialysis sessions were significantly higher in SVS patients. Patients with definitive SVS at the end of the follow-up (6 mo) (n = 12) also showed a higher number of inserted catheters, and longer time in place, than those without SVS or with recanalization of venous lesions (Table 2). Finally, catheter-related infections were twice as frequent in patients with definitive SVS (Table 2).

No differences in the incidence of SVS between patients with single (three of eight) and double lumen catheters (nine of 34) were observed at 6 mo. In addition, the incidence of

Table 1. Clinical characteristics of patients with or without subclavian vein stenosis at the time of baseline venography

Characteristic	Stenosis (n = 22)	No Stenosis (n = 20)
Age (yr)	47.8 ± 21.3	44.1 ± 16.7
Gender (M/F)	17/5	11/9
Side of catheterization	16R/6L	15R/5L
Days of catheterization	45.8 ± 35.8	22.6 ± 12.2[a]
No. of dialysis sessions	19.6 ± 15.3	9.75 ± 5.2[a]
Catheter lumen (single/double)	17/5	17/3
Total number of inserted catheters	1.5 ± 0.6	1.05 ± 0.2[a]
No. of patients with catheter-related infections (%)	12 (54.5%)	6 (30%)[b]
Catheter-related fever	6	1
Sepsis	4	2
Ipsilateral phlebitis + sepsis	1	0
Exit-site infection	1	3

[a] $P < 0.01$.
[b] $P = 0.07$.

Table 2. Comparison of patients with or without subclavian vein stenosis at the time of the venographic study performed 6 mo after catheter removal

Characteristic	Stenosis (n = 12)	No Stenosis (n = 30)
Age (yr)	53.2 ± 18.1	43.2 ± 19
Gender (M/F)	11/2	17/13[a]
Catheterization side (R/L)	9/3	22/8
No. of diabetic patients (%)	1 (8.3%)	9 (30%)
Total number of catheters placed	1.58 ± 0.6	1.2 ± 0.48[a]
Duration (days)	49.08 ± 32.2	29.03 ± 26.6[a]
No. of dialysis sessions	21 ± 13.8	12.4 ± 11.4[a]
Catheter lumen (single/double)	9/3	25/5
No. of patients with catheter-related infections (%)	8 (66.6%)	10 (33.3%)[a]
Catheter-related fever	3	4
Sepsis	3	3
Ipsilateral phlebitis + sepsis	1	0
Exit-site infection	1	3

[a] $P < 0.05$.

spontaneous recanalization was also similar with single (eight of 34) and double lumen catheters (two of eight). Finally, no differences were found in the analyzed parameters between patients with definitive SVS (n = 12) and those with spontaneous recanalization of the venous lesions (n = 10).

Discussion

SVS and thrombosis are important complications of the subclavian vein catheterization in acute hemodialysis. Most SVS are initially asymptomatic, but arm swelling and raised venous dialysis pressures occur with SVS after an ipsilateral arteriovenous fistula is created. The reported incidence of such lesions has ranged between 15 and 50% (3–12). However, spontaneous resolution of the venous lesions is possible. In fact, Spinowitz *et al.* (5) and van der Merwe *et al.* (4) observed that two of four and three of six patients in their respective studies presented recanalization of venous lesions after 30 d and 4 mo after removal, respectively, suggesting that early venous thrombosis can be transient.

Little is known about the natural history of SVS, particularly the optimal time period to perform a venographic study after catheter removal to rule out that SVS has not been established. In those studies reporting a venography after catheter removal, the time between removal and the radiologic study ranged from a few hours to 2 yr (4,5,7,8,10,12). As a result, if spontaneous resolution of subclavian thrombosis occurs during the first month after catheter removal, the true incidence of SVS might be overestimated when the venography is performed too early. Thus, a formal sequential venography study to determine the natural history of SVS is warranted.

In the present study, 52.4% of the patients showed SVS when the radiologic study was performed in the first month after catheter removal. However, half of the cases showed a normalization of the venous morphology in the study performed 3 mo after removal, and no changes were observed thereafter (sixth month). Thus, our findings indicate that 3 mo after removal is the optimal time period to perform a venographic study to exclude SVS in those patients who have had a subclavian acute vascular access. In addition, the creation of an ipsilateral arteriovenous fistula is possible in patients with SVS, but only after repeating the venogram 3 mo after catheter removal to check if recanalization has occurred. Finally, no patient with a normal baseline venogram showed abnormalities on subsequent radiographs, as it has been reported before by van der Merwe *et al.* (4). As a result, when SVS is not seen in the radiologic study immediately after catheter removal, the chance of a further SVS is negligible.

The final incidence of SVS in the present study was 28.6%. This value compares unfavorably with the reported low incidence of internal jugular vein stenosis after catheterization for hemodialysis (0 to 10%) (8,10,15,16). Therefore, our current practice has been modified and consists of the preferential use of the internal jugular vein for acute vascular access in hemodialysis patients.

The basic mechanisms that lead to SVS after cannulation are not well understood (5,6,8,17). A definite relationship between the incidence of SVS and the duration of catheterization has not been conclusively established. An association between the incidence of SVS and the duration of catheterization has been observed in two studies (7,18), although this has not been reported by others (5). Other factors such as mural thrombosis secondary to endothelial disruption, fibrosis caused by movement of the catheter in the venous lumen, leaking of plasticizer by the catheter itself, and catheter-related infections have all been associated with SVS (6–8,17).

In the present study, patients with definitive SVS showed a longer duration of catheterization and a higher number of inserted catheters. Catheter-related infection, the most common complication of subclavian dialysis catheter (19), was twice as frequent in patients with SVS, confirming our previously reported observations (12). The infection-induced local inflammatory process in the presence of a mechanically injured intima may induce fibrosis and ultimately vein stenosis. It remains to be determined whether antiplatelet therapy or antibiotic prophylaxis has a beneficial effect on the incidence of SVS.

In summary, 52% of patients whose subclavian vein is cannulated show stenosis or total thrombosis when a venography is systematically performed 24 to 48 h after catheter removal, or 4 wk later. Even when recanalization occurs in many instances, a definitive stenosis is seen in 28% of patients. Definitive lesions were observed by 3 mo after catheter removal. Thus, the creation of an ipsilateral vascular access is possible provided that venography is normal at this time. Finally, mechanical factors such as duration of catheterization and number of inserted catheters and dialysis sessions, together with catheter-related infection, are risk factors for SVS.

Acknowledgment

We are grateful to the paramedical personnel who made this study possible.

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