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Master's Thesis in
Medical Science

Assessment of venographic abnormalities during replacement of dysfunctional tunneled hemodialysis catheters and outcome of endovascular salvage techniques

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Assessment of venographic abnormalities during replacement of dysfunctional tunneled hemodialysis catheters and outcome of endovascular salvage techniques

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I submit this thesis as the Master’s thesis in Medical Science.

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The Master's thesis of Seon Young Park in Medical Science is hereby approved.

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December 21th, 2016
ABSTRACT

Assessment of venographic abnormalities during replacement of dysfunctional tunneled hemodialysis catheters and outcome of endovascular salvage techniques

Objectives: To assess the venography findings of central venous abnormalities before exchanging dysfunctional tunneled hemodialysis catheters and also to assess the outcome of endovascular salvage techniques.

Materials and Methods: From January 2011 to December 2015, seventy-eight patients (M:F, 33:45; mean age: 67 y; age range: 25-86 years) undergoing catheter-directed hemodialysis treatment were evaluated for 110 episodes of tunneled hemodialysis catheter dysfunction. Venography was performed through indwelling hemodialysis catheter pulled out to brachiocephalic vein before catheter exchange, and subsequent procedure was taken according to the venography findings - catheter exchange with or without tip position adjustment, balloon disruption of fibrin sheath, or angioplasty of venous stenosis or occlusion. Immediate evaluation of catheter function was manually performed at the intervention room after catheter exchange and technical success was defined as at least one successful session of hemodialysis with the exchanged catheter. Patients were followed up to the end-points or to the point of last hospital visit with evaluation of procedure associated complications such as catheter-related infection.

Results: Venography findings showed abnormalities in 67 out of 110 exchanged catheters; central vein stenosis in 27 (40.3%), fibrin sheath formation in 17 (25.4%), thrombus formation in 12 (17.9%), complex findings of more than two abnormalities in 9 (13.4%), and two cases of in-stent restenosis. Among sixty-seven abnormal venographycases, 34 catheters were exchanged with or without catheter tip position adjustment. Balloon disruption of fibrin sheath was performed in 9 cases and balloon angioplasty of central vein stenosis or occlusion was performed in 20 cases. Balloon was used for both fibrin sheath disruption and central venous angioplasty in 1 complex case and endovascular stent
was placed in 3 complex cases according to the indication. Manually assessed immediate catheter function was good in all cases and technical success was confirmed in all cases. During follow up, 29 catheters were lost to follow-up and the estimated 30-day catheter patency for all of the assessable catheters was 61.7%. Among assessable catheters showing abnormal venography findings, estimated 30-day catheter patency was 60.7% for catheter exchange with or without catheter tip position adjustment, 75% for balloon disruption of fibrin sheath, and 70% for balloon angioplasty of central vein stenosis or occlusion. Nine catheters were removed during the follow-up period due to suspected catheter-related infection, which was equivalent to 1.1 episodes/1000 catheter days. There were no other complications associated with the procedure. Thirteen patients revisited the intervention room due to 32 episodes of recurrent dysfunction of hemodialysis catheter, with most common reason being central vein stenosis, followed by complex cases of more than one abnormal venography findings.

**Conclusion:** About 60% of dysfunctional tunneled hemodialysis catheter showed abnormal venography findings, with central venous stenosis being the most common abnormality. Appropriate endovascular techniques were performed according to the venography findings and the catheter patency was comparable with previous reports regarding various techniques for the management of dysfunctional hemodialysis catheter, with low risk of procedure related complications.

**Keywords:** Dysfunctional tunneled hemodialysis catheter exchange, Venography, Endovascular salvage technique
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I. INTRODUCTION

Although the native arteriovenous fistula (AVF) is recommended as the first choice dialysis access for most patients with better outcomes (1-3), the usage of hemodialysis catheter is unavoidable in some patients; these include using catheter as a bridge before maturation of AVF or waiting for renal transplantation, and in elderly and diabetic patients having unsuitable vessels for AVF. The National Kidney Foundation (NFK)-Kidney Disease Outcome Quality Initiative (KDOQI) issued Clinical Practice Guidelines for Vascular Access in 2006 recommend that less than 10% of prevalent hemodialysis patients should be maintained on central catheters as their permanent dialysis access. However, catheter usage in prevalent hemodialysis was reported from 2% to 45% among 20 countries in 2013, in which most countries except Japan reported more than 10% usage of catheter as prevalent hemodialysis access (4).

There are several complications associated with tunneled hemodialysis catheters that can reduce catheter survival, including central vein stenosis, thrombus or fibrin sheath formation which can lead to catheter dysfunction causing inadequate dialysis, and catheter-related infection. Up to 52% of tunneled hemodialysis catheters are reported to be removed within one year due to catheter dysfunction and catheter-related infection, and some of the reports suggest catheter dysfunction as the main reason for non-elective removal (5-8). In these cases of catheter dysfunction, subsequent catheter replacement is mostly required, but prior catheter dysfunction itself is reported to be the strong predictor of hemodialysis catheter failure due to anatomical alterations in the central vein (5, 6), which may include pre-mentioned central vein stenosis, thrombus, or fibrin sheath formation.

Therefore, the purpose of this study was to assess the venography findings of central venous abnormalities before exchanging dysfunctional tunneled hemodialysis catheters and also to assess the outcome of endovascular salvage techniques.
II. MATERIALS AND METHODS

A. Patients

From January 2011 to December 2015, a total of 78 consecutive patients undergoing catheter-directed hemodialysis treatment for 110 episodes of tunneled hemodialysis catheter dysfunction were evaluated retrospectively. Tunneled hemodialysis catheter dysfunction was defined as inadequate dialysis session due to decreased blood flow rates (<300mL/minute) and frequent arterial and venous pressure alarms. The patient population included 33 men and 45 women, with a mean age of 67 years (median, 7 years; range, 25-86 years). Five patients were temporarily undergoing catheter-directed hemodialysis treatment in the setting of acute kidney injury; remaining seventy-three patients were using central catheter as their permanent dialysis access, mostly in the setting of established end-stage renal disease except in one patient, who underwent bilateral nephrectomy due to emphysematous pyelonephritis.

B. Techniques

The patients were placed on the angiography table and blunt dissection was performed under local anesthesia with 1% lidocaineHCl at indwelling catheter to free the cuff from the surrounding tissue at the exit site. Under fluoroscopic guidance, two 0.035-inch Terumo guidewires (Terumo Corp., Tokyo, Japan) were inserted each through double lumen of hemodialysis catheter with wire tips placed in the inferior vena cava (IVC). After partially withdrawing the catheter such that catheter tip was positioned at brachiocephalic vein level, 10ml of non-ionic contrast material (BonorexIohexol 350; CMS, Seoul, Korea) mixed with 5ml saline was injected manually and serial digital subtraction angiography (DSA) was performed. All the images were assessed by performing radiologist and categorized as normal and abnormal venography. Focal or segmental luminal narrowing of brachiocephalic vein or superior vena cava (SVC) was considered as central vein stenosis, thin contrast tracking along the catheter was considered diagnostic of fibrin sheath formation, and filling defects around the catheter or elsewhere inside the central vein was considered diagnostic as thrombus formation. Subsequent interventional procedure was
performed at the discretion of the performing radiologist according to the venography findings; catheter exchange with or without tip position adjustment, balloon disruption of fibrin sheath, or angioplasty of venous stenosis or occlusion. Endovascular stent was indicated in cases of recurrent or remaining venous stenosis after several sessions of balloon angioplasty. A new tunneled hemodialysis catheter was advanced over the wire under fluoroscopic guidance with the tips placed in appropriate position after one session of venography in normal cases and after repeated session of venography to confirm the resolution of problem in abnormal cases. Immediate evaluation of catheter function was manually performed at the intervention room with 20cc syringe ensuring adequate aspiration and forward flow on completion of catheter exchange.

C. Follow-up
Technical success was defined as at least one successful session of hemodialysis with the exchanged catheter. Catheters were removed if complication was encountered (mechanical problem, suspected catheter-related infection) and in these cases subsequent catheter exchange were performed into tunneled or non-tunneled catheters according to patient status. Catheters were also removed in cases where they were no longer needed (AVF maturation, recovery of native kidney function, renal transplantation, patient death), or in cases when patient refuses to keep catheters. They were followed up to one of these endpoints or to the point of last hospital visit. The reason for catheter removal, the duration of catheter up to the point of removal or to the last hospital visit were recorded. Complications were classified as major and minor according to SIR classifications, with catheter-related infection included as major(9). These complications were evaluated by reviewing the medical records and laboratory findings. This retrospective study was approved by our institutional review board and the requirement for informed patient consent was waived.
III. RESULTS

Venography findings were considered abnormal in 67 out of 110 exchanged catheters (60.1%); central vein stenosis in 27 (40.3%, out of 67 abnormal venography), fibrin sheath formation in 17 (25.4%), thrombus formation in 12 (17.9%), complex findings of more than two abnormalities in 9 (13.4%), and two cases of in-stent restenosis where central venous stenting was done previously [table1]. Additionally, simple fluoroscopic images taken before withdrawal of dysfunctional catheter revealed inappropriate positioning or wedging of the catheter in 4 cases among 43 catheters showing normal venography findings [figure 1].

Among 67 abnormal venography cases, 34 catheters were exchanged with or without catheter tip position adjustment. Balloon disruption of fibrin sheath was performed in 9 cases and balloon angioplasty of central vein stenosis or occlusion was performed in 20 cases. Balloon was used for both fibrin sheath disruption and central venous angioplasty in one complex case showing combination of fibrin sheath formation and central vein stenosis. Endovascular stent was placed in 3 cases according to the indication, which were all complex cases [figure 2-5]. All of the catheters showing normal venography findings were simply exchanged with or without catheter tip position adjustment. Manually assessed immediate catheter function was good in all cases and technical success was confirmed in all cases.

Among exchanged 110 catheters, 29 catheters were lost to follow-up returning to referring hospital after the procedure, and remaining 81 catheters were followed up to the point of removal or to the point of their last hospital visit. The estimated 30-day catheter patency was 61.7% for all of the assessable catheters, and among them, 63% for catheters showing abnormal venography findings and 59.3% for catheters showing normal venography. Among assessable catheters showing abnormal venography findings, estimated 30-day catheter patency for each interventional procedures are as follows; 60.7% for catheter exchange with or without catheter tip position adjustment, 75% for balloon disruption of fibrin sheath, and 70% for balloon angioplasty of central vein stenosis or occlusion. The mean follow-up duration per catheter was 74.8 days (range, 3-389 days).
with 67 catheters (82.7%) removed and 14 catheters (17.3%) still functioning at the end of
the study with mean duration of 96 days (range, 25-321 days). The reasons for catheter
removal are listed in Table 2. The most common reason for catheter removal was catheter
dysfunction, in 31 out of 67 removed catheters (46.3%). Other reasons for catheter removal
included maturation of AVF in 11 (16.4%), suspected catheter-related infection in 9
(13.4%), mechanical catheter problems such as catheter dislodgement and injury in 7
(10.4%), patient death in 5 (7.5%), patient refusal in 2 (3%) and each one cases of renal
transplantation and recovery of native kidney function. The removed 9 catheters due to
suspected catheter-related infection were equivalent to 1.1 episodes/1000 catheter days.

During the follow-up period, 32 re-intervention episodes were required in 26
catheters (38.8%, out of 67 removed catheters) due to recurrent catheter dysfunction,
involving 13 patients with 30-day catheter patency of 53.8%. The most common reason for
recurrent catheter dysfunction was central vein stenosis, followed by complex cases of
more than one abnormal venography findings. More than one re-intervention was required
in 8 patients (five required two, one required three, and two required more than three re-
interventions). The maximum number of re-intervention was eight in one patient over the
span of 11 months.
Table 1. Venography findings

| Venography findings                  | N   | %   |
|--------------------------------------|-----|-----|
| Abnormal                             |     |     |
| Central vein stenosis                | 21  | 40.3|
| (67/110, 60.1%)                      |     |     |
| Fibrin sheath formation              | 17  | 25.4|
| Thrombus formation                   | 12  | 17.9|
| Complex*                             | 9   | 13.4|
| In-stent restenosis                  | 2   | 3   |
| Normal                               |     |     |
| With mechanical problem              | 4   | 9.3 |
| (43/110, 39.9%)                      |     |     |
| Without mechanical problem           | 39  | 90.7|

* Two or more combined findings of central vein stenosis, fibrin sheath formation, thrombus formation

Table 2. Reason for catheter removal

| Reason for removal                  | N   | %   |
|--------------------------------------|-----|-----|
| Dysfunction                          | 31  | 46.3|
| AVF maturation                       | 11  | 16.4|
| Infection                            | 9   | 13.4|
| Mechanical problem*                  | 7   | 10.4|
| Patient death                        | 5   | 7.5 |
| Others**                             | 4   | 6   |

* Catheter dislodgement, injury, leakage
** Patient refusal, renal transplantation, recovery of native kidney function
Figure 1 Normal venography findings in 75-year-old male. The patient was managed with simple catheter exchange over the wire without additional intervention.

Figure 2 A. Venography reveals central vein stenosis at junction of SVC-RA in 68-year-old female. B. The patient was managed with catheter exchange over the wire with adjustment of catheter tip position, avoiding the site of central vein stenosis.
Figure 3 51-year-old female A. Venography reveals fibrin sheath limiting contrast flow along the catheter insertion pathway. B, C. Balloon angioplasty was performed to rupture the fibrin sheath. Note the waist formation at the balloon during partial inflation (arrow). D. Repeated venography after the intervention no longer visualizes contrast flow limitation.

Figure 4 45-year-old female A. Venography reveals central vein stenosis at SVC level. B. Balloon angioplasty was C. Repeated venography after the intervention reveals improved stenosis at SVC level.
Figure 581-year-old female A. Venography reveals complex findings of central vein stenosis at SVC level (arrow) with fibrin sheath along catheter insertion pathway (arrowheads). B. Stenosis of SVC remained after several sessions of balloon angioplasty (not seen), and stent was placed in the SVC despite the fact the patient had cardiac pacemaker installed. C. Repeated venography after the intervention reveals improved stenosis and disappearance of fibrin sheath. D. New catheter was inserted over the wire and lasted for 47 days.
IV. DISCUSSION

Hemodialysis catheter dysfunction is reported to be one of the main reasons for non-elective removal of hemodialysis catheter, with requirement of subsequent catheter exchange. This creates disadvantages for the patients with increased cost and increased morbidity (5-8, 10). In current study, mechanical problems such as catheter malposition or wedging was much less common than other well established causes of catheter dysfunctions such as central venous stenosis, fibrin sheath formation, and thrombus formation, which is consistent with previous studies (11).

There have been variety of techniques described for the management of dysfunctional hemodialysis catheter resulting from causes other than mechanical problems in past years, including conservative method using thrombolytic agents to dissolve fibrin clots and thrombus, which has been described for almost 30 years (12). However, with the emerging issues of thrombolytic therapy becoming refractory with recurrent flow problems in cases of persistent thrombus and fibrin sheath (13), fibrin sheath stripping was discovered as an alternative endovascular technique, followed by other techniques such as catheter exchange over the wire and balloon disruption of fibrin sheath. The reported success rates of these techniques vary with each study, and controversy remains regarding their outcomes. Our 30-day catheter patency rates for abnormal and normal venography cases (59.3-63%) are in the range of those previous reports regarding various techniques for the management of dysfunctional hemodialysis catheter (43.9-76.1%) (14-20).

Venography was also performed in most of the previous reports for assessment of underlying cause of catheter dysfunction, through indwelling catheter either in the original place or pulled back. The difference between prior studies and current study is that venography was optional in prior studies with some portion of study population not receiving venography due to suspected infection or other miscellaneous reasons, while venography was performed in all cases of dysfunctional catheter exchange in current study. The rate of abnormal venography findings was 60.1% in current study, which is within range of 47-79% reported in previous studies (10, 11, 16, 19-22).
The estimated 1.1 catheter-related infection episodes/1000 catheter days in current study is lower than previously reported catheter-related infection rates, which were 1.42-5.2 episodes/1000 catheter days (23-25). Five patients expired and had catheter removed during the follow-up period. Simple catheter exchange over the wire was performed in four patients and one patient received balloon angioplasty at central vein due to thrombus formation. Most of the deaths happened after more than one week of catheter exchange, suggesting low possibility of procedure-related morbidity. One patient who expired after three days from catheter exchange was in the setting of acute kidney injury due to sepsis and the death was thought to be attributed to septic shock. There was no other evidence of morbidity or mortality, suggesting that performing venography and subsequent intervention with catheter exchange over the wire is safe and has low risk of catheter-related infection or other complications.

Our study has limitations. First, it was a retrospective study with relatively small patient population. Also, patients were allowed to enroll more than once, since all dysfunctional hemodialysis catheter exchange cases were included in the study regardless of the presence of previous experience of catheter dysfunction. The outcome of the exchanged catheter was considered to be independent of the previous catheter, and the proportion of cases having repeated catheter dysfunction leading to repeated re-interventions was not low. As reported in previous study, the presence of previous experience of hemodialysis catheter insertion and/or dysfunction may play as the most powerful predictor of hemodialysis catheter dysfunction (5), and it may have affected the catheter patency rate presented in current study. Lastly, due to the fact that our institution is a tertiary referral center, some portion of study cases were lost to follow-up after the procedure, and substantial portion of study cases had to be assumed for successful session of hemodialysis by having no more referrals issuing catheter dysfunction.
V. CONCLUSION

In conclusion, about 60% of dysfunctional tunneled hemodialysis catheter showed abnormal venography findings, with central venous stenosis being the most common abnormality followed by fibrin sheath formation. Appropriate endovascular techniques were performed according to the venography findings and the catheter patency was comparable with previous reports regarding various techniques for the management of dysfunctional hemodialysis catheter. Also, the rate of complications such as catheter-related infections was low. These findings implicate that performing venography before exchange of dysfunctional tunneled hemodialysis catheter with subsequent appropriate act could be helpful in improving catheter patency with low risk of procedure-related complications.
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국문 요약

기능부전 터널식 투석용 도관의 교체 시 시행한 정맥조영술 결과의 분석과 혈관 내 치료 기술의 결과

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연구 목적: 기능부전 터널식 투석용 도관의 교체 전에 시행한 정맥조영술의 결과를 분석하고 이에 따른 혈관 내 치료 기술의 결과에 대하여 알아보고자 한다.

연구 대상 및 방법: 2011년 1월에서 2015년 12월 사이에 터널식 투석용 도관을 통한 투석을 받고 있으며 터널식 투석용 도관의 기능부전이 있어서 투석용 도관의 교체를 시행 받은 78명의 환자를 대상으로 후향적으로 연구한다. 투석용 도관의 교체 전에 도관의 끝을 팔마리동맥 정도까지 위치시키고 정맥조영술을 시행한다. 정맥조영술의 결과에 따라 적절한 중재 시술을 시행하며 이에는 투석용 도관의 끝 위치 조정을 하거나 하지 않고 도관의 교체를 시행하는 것, 풍선을 이용한 섬유소집 (fibrin sheath)의 파열, 그리고 중심 정맥의 혈착 또는 폐색에 대한 혈관성형술이 포함된다. 투석용 도관의 교체 직후 혈관조영술에서 수동적으로 도관의 기능을 평가하고 기술적 성공은 투석용 도관 교체 후 적어도 한 번 이상의 성공적인 투석의 진행으로 정의한다. 환자들은 도관의 제거일 또는 마지막 병원 방문일 까지 추적 관찰하고 시술과 관련된 합병증에 대하여 평가된다.

연구 결과: 총 110개의 교체된 기능 부전 터널식 투석용 도관이 연구에 포함되었고, 그 중 67개의 도관의 교체 전 정맥조영술에서 비정상적인 소견이 나타났다. 중심 정맥의 혈착이 27건 (40.3%), 섬유소집 (fibrin sheath)의 형성이 17건 (25.4%), 혈전의 형성이 12건 (17.9%), 두 개 이상의 비정상 소견이 병합된 경우가 9건 (13.4%)이 있었고 나머지 두 건은 혈관 내관 (stent)이 있는 상태에서 내관 내에 재 혈착이 일어
난 경우였다. 비정상적인 정맥조영술 소견이 보인 67개의 도관 중 34개의 도관에서 교체를 시행하였고 9개의 도관에서 풍선을 이용한 섬유소집(fibrin sheath)의 파열을, 20개의 도관에서 풍선을 이용하여 중심 정맥의 협착 또는 폐쇄에 대한 혈관성형술을 시행하였다. 또한 두 개 이상의 복합된 비정상 정맥조영술 소견이 보였던 도관 중 한 개의 도관에서는 풍선을 이용하여 섬유소집(fibrin sheath)의 파열과 중심 정맥의 협착에 대한 혈관성형술을 동시에 시행하였고, 세 개의 복합된 소견이 보였던 도관에 대해서 혈관 내관(stent)을 설치하였다. 추적 관찰 도중 29개의 도관에 대한 추적은 실시되었고 나머지 추적이 가능한 도관들의 30일 도관 생존율은 61.7%였다. 비정상 정맥조영술 소견이 보였던 도관들 중 추적 가능한 도관들의 30일 도관 생존율은 각각 교체를 시행한 경우 60.7%, 풍선을 이용한 섬유소집(fibrin sheath)파열을 시행한 경우 75%, 그리고 중심 정맥의 협착 또는 폐쇄에 대한 혈관성형술을 시행한 경우 70%였다. 추적 기간 동안 9개의 도관에서 도관감염이 의심되어 도관의 제거를 시행하였고 이는 1.1사건/1000도관일로 상응하였다. 이 외에 시술과 관련하여 발견된 합병증은 없었다. 13명의 환자가 32건의 반복된 도관의 기능부진으로 다시 혈관조영실을 방문하였고 반복된 기능부전의 가장 혼란 원인은 중심정맥의 협착이었다.

연구 결론: 기능 부전 터널식 투석용 도관의 교체 시 약 60%에서 비정상적인 정맥조영술 소견이 관찰되었으며 가장 혼란 소견은 중심 정맥의 협착이었다. 이러한 소견에 대하여 적절한 혈관 내 중재술을 시행한 결과 도관의 생존율은 이전에 기능부전 터널식 투석용 도관의 치료에 대하여 여러 가지 방법을 실험하였던 연구들과 비견할 만하다으며 시술과 관련된 합병증의 위험도는 낮았다.

핵심어: 기능부전 터널식 투석용 도관의 교체, 정맥조영술, 혈관 내 치료 기술