Prevalence of Central Vein Stenosis in Patients Referred for Vein Mapping

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Abstract

Background and objectives Central vein stenosis is considered to be common in patients on hemodialysis but its exact prevalence is not known. In this study, we report the prevalence of central vein stenosis in patients with CKD referred for vein mapping.

Design, setting, participants, & measurements We conducted a retrospective study of adult patients who had bilateral upper extremity venographic vein mapping from September 1, 2011 to December 31, 2015. Patients with and without stenosis were compared for differences in clinical or demographic characteristics. Multiple logistic regression was used to identify independent associations between patient characteristics and central vein stenosis.

Results There were 525 patients who underwent venographic vein mapping during the study period, 27% of whom were referred before initiation of hemodialysis. The mean age (±SD) and body mass index were 59 (±15) years and 28 (±7), respectively. Women accounted for 45% of patients; 82% were black. The prevalence of central vein stenosis was 10% (95% confidence interval [95% CI], 8% to 13%) for the whole group, and 13% (95% CI, 10% to 17%) among patients with tunneled central venous dialysis catheters. Current use of tunneled hemodialysis catheters (odds ratio [OR], 14.5; 95% CI, 3.25 to 65.1), presence of cardiac rhythm devices (OR, 5.07; 95% CI, 1.82 to 14.11), previous history of fistula or graft (OR, 3.28; 95% CI, 1.58 to 6.7), and history of previous kidney transplant (OR, 18; 95% CI, 4.7 to 68.8) were independently associated with central vein stenosis.

Conclusions In this population, the prevalence of central vein stenosis was 10% and was clustered among those with tunneled hemodialysis catheters, cardiac rhythm device, and previous history of dialysis access or transplant.


Introduction

Current guidelines recommend referral of patients with CKD for specialty care, including evaluation for placement of permanent hemodialysis access when need for kidney replacement therapy is expected within a year (1,2). Preoperative assessment of upper extremity veins with ultrasonography or venography may reduce likelihood of immediate fistula failures or unsuccessful surgical exploration (3,4). Which of these two imaging modalities produces superior dialysis access outcomes has not been studied, but its noninvasive nature, avoidance of radiocysternograph and ability to examine arterial anatomy have made Duplex ultrasound a preferred method of vascular mapping, except in patients with risk factors for central vein stenosis (2,5). The sensitivity and specificity of Duplex ultrasound for diagnosing central vein stenosis, however, are limited and venography remains the gold standard for evaluation of central vein patency (6,7).

Prevalence of central vein stenosis ranging from 9% to as high as 51% has been reported in patients on hemodialysis (8–16). An important shortcoming of most of these studies is that vascular imaging was performed for clinical indications such as symptomatic venous hypertension, dialysis access dysfunction, or history of hemodialysis catheter placement. The indications for vascular imaging, therefore, could introduce a source of bias because patients on hemodialysis without central vein stenosis are more likely to be underrepresented, and those with central vein stenosis more likely to be overrepresented, than would be seen in a group of unselected patients on hemodialysis (17).

Preoperative mapping venography might not be prone to confounding by indication because the need for creation of a permanent hemodialysis access is not directly related to the likelihood of having central vein stenosis unless the imaging technique is selectively used for patients at a higher risk of central vein stenosis. Our program’s use of venography as the primary modality of vein mapping provided an opportunity to reexamine prevalence of central vein stenosis. Herein, we report findings of a retrospective study of a large unselected cohort of patients with advanced CKD who underwent vein mapping by venography. Reliable assessment of the prevalence of and risk factors for central vein stenosis in patients with CKD has the potential to provide information on the magnitude of the problem, guide selection of appropriate imaging modality for vein mapping, and possibly improve clinical outcomes.
Materials and Methods

Design, Setting, and Participants

We conducted a retrospective chart review of all patients referred for vein mapping to the Dialysis Vascular Access program of State University of New York Downstate Medical Center from September 1, 2011 to December 31, 2015. The program serves patients at two teaching hospitals (University Hospital of Brooklyn and Kings County Hospital Center), their affiliated dialysis units, and dialysis units and nephrology practices in the surrounding area. Planning, creation, and maintenance of hemodialysis accesses are carried out by a multidisciplinary team consisting of dialysis access coordinators, interventional nephrologists, and transplant and vascular surgeons.

All adult patients who underwent bilateral upper extremity venogram were included in the study. Patients who had sonographic vein mapping or unilateral upper extremity venogram were excluded. We excluded patients with unilateral venograms because absence of information on the contralateral side could underestimate the true prevalence of central stenosis in the entire group. The Institutional Review Board of State University of New York Downstate Medical Center granted waiver of the privacy provisions of the Health Insurance Portability and Accountability Act; the dataset was collected without identifiers and thus deemed by the Institutional Review Board to be exempt from informed consent requirements and continuing review.

Vein Mapping Procedure

The program uses venography as the primary imaging modality for vein mapping. Venography of peripheral veins was performed by injecting half-strength radiocontrast under fluoroscopy through an intravenous cannula inserted into a superficial vein on the dorsum of each hand. Central vein imaging was performed with full-strength contrast using digital subtraction angiography. To avoid misdiagnosis of fluctuations in diameter of central veins with respiration as central vein stenosis, venography was performed during both inspiration and expiration. Stenosis was diagnosed if there was luminal narrowing of ≥50% by visual inspection, observed in both phases of respiration. Sonography was used if patients had a history of severe contrast reaction or expressed preference for sonography over venography, or peripheral vein cannulation was not possible.

Data Sources and Collection

Clinical notes provided by referring nephrologists, structured intake form at the time of the procedure, and reports of venography were reviewed. Data elements abstracted from these sources were as follows: age; sex; height; weight; presence or absence of diabetes mellitus, hypertension, or SLE; prior creation of fistula or graft; prior kidney transplant; type of insurance (public [Medicaid or Medicare] or private); stage of CKD; presence or absence of central vein stenosis, tunneled hemodialysis catheter, or cardiac rhythm device; and side of central stenosis or tunneled hemodialysis catheter, if applicable.

Statistical Analyses

Prevalence of central vein stenosis and its confidence interval were estimated by the normal approximation of the binomial distribution. Comparison of variables between patients with and without central vein stenosis was made using t test for continuous variables and chi-squared or Fisher exact test for categorical variables, as appropriate. Association between possible risk factors and central vein stenosis was evaluated with logistic regression, with adjustment for sociodemographic and clinical variables. Statistical procedures were not used to address missing data because variables had low level (0%-4%) of missing data. Two-tailed P values <0.05 were considered statistically significant. Statistical analysis was performed with IBM SPSS Statistics for Windows, version 24 (IBM Corp., Armonk, NY).

Results

A total of 658 patients underwent vein mapping during the study period, of which 133 were excluded; 113 were excluded because vein mapping was done with sonography and 20 because they only had unilateral venograms (Figure 1). For the final study sample of 525 patients, mean age (±SD) and body mass index (BMI) were 59 (±15) years and 28 (±7), respectively. Women accounted for 45% of patients; 82% were black, 8% were Hispanic, and 2% were white. All but three patients had no functional fistula or graft at the time of venography; the three patients had recurrent access dysfunction and were imaged in preparation for a new access. Approximately one quarter (27%) were referred for vein mapping before initiation of hemodialysis. Three quarters (76%) had public insurance, with 44% having Medicare and 32% Medicaid as their primary health insurance. The proportion of patients who had history of hypertension, diabetes, previous graft or fistula, prior kidney transplant, or lupus was 90%, 55%, 18%, 5%, and 3%, respectively; 26 (5%) presented with transvenous cardiac rhythm devices.

The prevalence of central vein stenosis was 10% (95% confidence interval [95% CI], 8% to 13%) for the entire group, and 13% (95% CI, 10% to 17%) among patients with a tunneled hemodialysis catheter. Table 1 shows comparison of clinical and demographic characteristics between patients with and without central vein stenosis. The group with central stenosis had statistically higher proportion of tunneled hemodialysis catheters (94% versus 69%), transvenous cardiac rhythm devices (15% versus 4%), and history of previous graft or fistula (43% versus 15%) or prior kidney transplant (19% versus 3%) compared with the group without central vein stenosis. In contrast to other studies, the proportion of patients with stenosis ipsilateral to the left-sided catheter (67%) was not statistically different from that of right-sided catheters (80%; P=0.47, Fisher exact test) (13,18).
Multiple logistic regression analysis identified independent association between central vein stenosis and current use of tunneled hemodialysis catheter (odds ratio [OR], 14.5; 95% CI, 3.25 to 65.1), presence of cardiac rhythm devices (OR, 5.07; 95% CI, 1.82 to 14.11), previous history of fistula or graft (OR, 3.28; 95% CI, 1.58 to 6.7), and history of previous kidney transplant (OR, 18; 95% CI, 4.7 to 68.8) (Table 2).

Central vein stenosis was not detected in any of the 117 patients who did not have tunneled hemodialysis catheter, transvenous cardiac rhythm device, or history of dialysis graft or fistula. Seven out of ten (70%) patients with previous kidney transplant also had history of graft or fistula. Of note, only three (2%) of the 141 patients who were predialysis had central vein stenosis.

### Discussion

Identification of suitable veins for fistula creation and confirmation of patency of central veins draining the access arm are critical first steps in planning for maintenance hemodialysis. In a study of a large group of unselected patients with advanced CKD who were evaluated with venography, we found an overall prevalence of central vein stenosis of 10% (95% CI, 8% to 13%), and only slightly higher prevalence (13%; [95% CI, 10% to 17%] among patients with tunneled hemodialysis catheters who were dialysis dependent.

The prevalence of central vein stenosis in our cohort is similar to estimates in some studies, but is lower than what is reported in several others. Specifically, prevalence of central stenosis in the range of 9%–12% has been reported involving catheterization of the right internal jugular vein and high-flow fistulas in the absence of history of catheterization (8,10,13), whereas higher prevalence (27%–51%) has been found in association with dysfunctional fistulas or grafts and catheterization of the left internal jugular vein or the subclavian vein (8,9,13,14). There could be several possible explanations for the variations between studies. First, the populations as well as the distribution of risk factors are likely different among studies. For example, it is possible that the location and number of catheters, or average access flow could be different between studies. Second, as mentioned above, studies in which venography is performed for clinical indications may tend to overestimate prevalence. Third, high blood flow through dialysis fistulas and grafts could produce symptomatic venous hypertension and/or accentuate radiologic findings that would have been less apparent in the absence of dialysis fistulas or grafts—a phenomenon particularly associated with upper arm accesses (14,19,20).

Consistent with existing literature, we found use of tunneled hemodialysis catheters or transvenous cardiac rhythm devices, and history of previous graft or fistula to be independent risk factors for central venous stenosis.
possible that these patients had had invasive vascular access. The reason for this association is not clear. It is instrumentation of veins or history of previous dialysis procedures that were not captured in their records.

vein stenosis in our cohort even after adjustment for demographics, use of subclavian or left internal jugular vein (as compared with right internal jugular), and longer dwell times (8,9,12,13,18). We did not, however, find higher risk of stenosis with catheterization of the left internal jugular vein. Wang et al. (13) estimated incidence of stenosis among patients with hemodialysis catheters at 0.68/1000 catheter-days. Although their estimate is on the basis of a cohort predominantly exposed to temporary catheters, it emphasizes the importance of catheter dwell time in the association between catheters and central vein stenosis. Because date of insertion of catheters was not available for our study, difference in catheter dwell time between patients in our cohort and those reported in other studies may in part explain the absence of association between left internal jugular vein catheterization and stenosis. Another possible explanation is the low rate of left internal jugular vein catheterization (13% of catheters) in our cohort.

Small cross-sectional studies have reported prevalence of central vein stenosis of 50%–70% in patients with cardiac rhythm devices who were on hemodialysis (22,23). By contrast, a prospective study involving serial venograms in patients with cardiac rhythm devices who were not on dialysis found a 14% incidence of central vein stenosis or occlusion at 6 months, with further but less steep incidence over the following 18 months (24). Possible explanations for the difference in prevalence between our cohort and prior reports are differences in population or study design, device dwell time, presence or absence of dialysis fistulas or grafts, and instability of estimates derived from small samples.

Strong association with central vein stenosis should caution against the trend of increasing use of cardiac rhythm devices in patients with CKD (25,26). Implantable cardioverter defibrillators reduce mortality in patients on dialysis who had cardiac arrest (27). Unlike patients without kidney failure, the role of implantable cardioverter defibrillators in primary prevention of sudden cardiac

| Table 2. Crude and adjusted odds ratio of risk factors for central vein stenosis |
|-----------------|-----------------|-----------------|-----------------|
|                 | Unadjusted OR  | 95% CI          | P Value |
|                 | Adjusted a OR  | 95% CI          | P Value |
| Age, per 10 yr | 0.88            | 0.72 to 1.07    | 0.19    |
| Women           | 0.92            | 0.52 to 1.63    | 0.77    |
| Body mass index | 0.95            | 0.9 to 1        | 0.54    |
| Primary insurance |                |                 |         |
| Private         | Ref             |                 |         |
| Medicare        | 1.51            | 0.71 to 3.22    | 0.23    |
| Medicaid        | 1.18            | 0.52 to 2.71    | 0.69    |
| Current tunneled catheter | 7.4 | 2.3 to 24.1 | 0.001 | 14.5 | 3.25 to 65.1 | <0.001 |
| Cardiac rhythm device | 4.5 | 1.85 to 10.9 | 0.001 | 5.07 | 1.82 to 14.11 | 0.002 |
| Previous fistula or graft | 4.24 | 2.3 to 7.7 | <0.001 | 3.28 | 1.58 to 6.7 | 0.001 |
| Previous transplant | 7.3 | 3.1 to 17.5 | <0.001 | 18 | 4.7 to 68.8 | <0.001 |

OR, odds ratio; 95% CI, 95% confidence interval; Ref, reference value.

aAdjusted for hypertension, diabetes, and SLE, in addition to the predictors listed in the table.
death, which accounts for most of the recent increase in use of such devices in patients on dialysis, is much less certain (26). Until additional data that clarify indications for implantable cardioverter defibrillators in the dialysis population are available, use of leadless pacemakers and defibrillators, or devices with epicardial rather than transvenous leads would be appropriate in those patients suitable for these kinds of devices (23,28).

Central vein stenosis could occur in the absence of central vein instrumentation due to extrinsic compression by narrow thoracic inlet, dilated arteries, or benign or malignant growths in adjacent structures (7,20,21). In addition, reports of central vein abnormalities or stenosis in patients on hemodialysis without history of catheters have given rise to the hypothesis that high blood flow rates through fistulas or grafts could directly cause endothelial injury, which in turn leads to neointimal proliferation and stenosis (10,29–31). There were no cases of central vein stenosis in this study in the absence of the risk factors we identified. This is in contrast to some studies that reported prevalence of central vein abnormalities ranging from 6% to 63% in patients without obvious risk factors for stenosis (7,10–12,30). Although factors such as extrinsic compression or hemodynamic stress could contribute to central vein stenosis, our data suggest that their contribution to prevalence of central vein stenosis in the general population of patients with advanced CKD may be less important than previously reported.

It is important to highlight the limitations of our study. First, the retrospective design did not allow collection of important variables such as catheter dwell time, and the number or type of invasive vascular procedures that might have been performed on the study participants. Second, a number or type of invasive vascular procedures that might be important variables such as catheter dwell time, and the number or type of invasive vascular procedures that might have been performed on the study participants. Second, a number or type of invasive vascular procedures that might have been performed on the study participants. Second, a number or type of invasive vascular procedures that might have been performed on the study participants. Second, a number or type of invasive vascular procedures that might have been performed on the study participants. Second, a number or type of invasive vascular procedures that might have been performed on the study participants. However, we did not image pelvic and abdominal veins, so our results refer only to prevalence of stenosis of intrathoracic veins.

In conclusion, we evaluated an unselected group of patients with advanced CKD with direct venography and found the prevalence of central vein stenosis to be lower than what has been previously reported, even among patients with hemodialysis catheters. Central veins stenosis was clustered among patients with tunneled hemodialysis catheter, cardiac rhythm device, and previous history of dialysis access or transplant. These risk factors should be considered in deciding the need for venographic vein mapping. Our findings also emphasize the importance of avoiding instrumentation of central veins in patients with CKD whenever possible. Future studies in a representative group of patients with advanced kidney disease should examine not only the mechanisms underlying central vein stenosis, but also whether patients who do not develop stenosis have protective factors that promote favorable outcomes.

Disclosures
None.

References


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