Impact of Previous Tunneled Vascular Catheters and their Location on Upper Limb Arteriovenous Fistula Function

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Key Points
- Previous TVC use was associated with poorer AVF function at 6 and 12 months, compared with no prior TVC use.
- The presence of an ipsilateral TVC was associated with lower successful AVF use at 6 months, compared with contralateral TVC.
- Previous TVC use was associated with higher rate of assisted maturation, compared with no prior TVC use.

Abstract
Background Long-term arteriovenous fistula (AVF) survival has been shown to be adversely affected by the presence of previous tunneled vascular catheters (TVC). We analyzed the effect of previous TVCs and their location (ipsilateral versus contralateral) on the successful function of upper-limb AVFs in the first 12 months after creation.

Methods We retrospectively reviewed clinical data on patients’ first upper-limb AVFs, created between January 2013 and December 2017. We analyzed the rates of successful AVF function (successful cannulation using two needles for ≥50% sessions over a 2-week period) at 6 and 12 months after creation, time to AVF maturation, and rates of assisted maturation.

Results In total, 287 patients with first AVFs were identified, of which 142 patients had a previous TVC (102 contralateral, 40 ipsilateral) and 145 had no previous TVC. The no TVC group had higher rates of AVF function at both 6 months (69% versus 54%, OR, 1.84; 95% CI, 1.00 to 3.39, P = 0.05) and 12 months (84% versus 64%, OR, 3.10; 95% CI, 1.53 to 6.26, P = 0.002) compared with the TVC group. The contralateral TVC group had higher rates of AVF function at 6 months (60% versus 40%, OR, 2.21; 95% CI, 1.01 to 4.88, P = 0.05), but not at 12 months (66% versus 58%, OR, 1.42; 95% CI, 0.62 to 3.25, P = 0.40) compared with the ipsilateral TVC group. The median time to AVF maturation in the contralateral and ipsilateral TVC groups were 121.5 and 146 days respectively (P = 0.07).

Assisted maturation rates were lower in no TVC group compared with the TVC group (12% versus 28%, P = 0.007), but similar between the contralateral and ipsilateral TVC groups (29% versus 26%, P = 0.74).

Conclusions Previous TVC use was associated with poorer AVF function at 6 and 12 months, with a higher rate of assisted maturation. The presence of an ipsilateral TVC was associated with lower successful AVF use at 6 months, compared with contralateral TVC.

Introduction
The 2019 Kidney Disease Outcomes Quality Initiative Vascular Access Guidelines generally recommend a “fistula-first” approach to prepare patients for the initiation of hemodialysis (1). This is on the basis of evidence demonstrating that patients starting hemodialysis with an arteriovenous fistula (AVF) have lower morbidity and mortality, lower complications (including bloodstream infections), and achieve higher blood flow rates compared with patients initiating dialysis with a tunneled vascular catheter (TVC) (1). The Standardized Outcomes in Nephrology for Hemodialysis ranked adequate vascular access function as the top priority for both patients and health professionals alike (2). The triad of AVF maturation, function, and survival are essential to the patient’s successful long-term hemodialysis management (3).

Approximately one third to half of all created AVFs fail to mature. Advanced age, diabetes, and vascular disease are comorbidities associated with poorer AVF outcomes (4). Furthermore, outcomes of AVFs are inferior in patients with a previous TVC insertion.
One study reported the risk of AVF failure was 81% higher in patients with prior temporary vascular catheter access (5). Mechanical injury from catheter insertion and continuous catheter movement within the vessel can lead to endothelial damage, inflammation, and intimal hyperplasia or fibrosis (6,7). Subsequent catheter-induced stenosis of the central veins has been thought to lead to the poor maturation, function, and eventually reduced survival of subsequently formed AVFs (8).

Some retrospective studies have also shown that long-term AVF survival is lower in patients with previous ipsilateral TVC, compared with contralateral TVC (9). However, the effect of an existing TVC and its location on the subsequently formed AVF’s maturation and early function has not been well studied. It is well recognized that AVFs that are slow to mature and require early or assisted maturation are associated with poorer long-term survival (10). We aimed to analyze the effect of a previous TVC and its location (contralateral or ipsilateral to AVF) on the successful function of the patient’s first AVF at 6 and 12 months after creation. We also analyzed the rates of assisted maturation and time to first successful use.

**Materials and Methods**

**Data Collection**

In this single-center, retrospective, observational cohort study, we collected data on all patients aged >18 years with CKD or ESKD who had their first upper-limb AVF created between January 2013 and December 2017, and identified those who had a TVC inserted before the AVF creation. Lower-limb AVFs, arteriovenous grafts, second, and subsequent AVFs were not included in the analysis. Data were collected from a vascular access database and the individual patient’s electronic medical records. Ethics approval was obtained from our institutional ethics board.

**Patients**

A total of 287 patients had their first upper-limb AVF created. Of these, 142 patients had a TVC inserted, either contralateral (n=102) or ipsilateral (n=40), before subsequent AVF creation. One patient had both left- and right-sided previous TVC insertions, and was categorized as ipsilateral. A total of 145 patients had no previous TVC insertion at the time of AVF creation. Of these, four patients were already on peritoneal dialysis at the time of AVF creation. As per local policy, AVFs were monitored 4–6 weeks after the procedure with a Doppler ultrasound and vascular surgeon review. Assisted maturation procedures were performed at the discretion of the vascular surgeon on the basis of clinical examination and ultrasound findings. All TVCs were inserted using ultrasound and fluoroscopic guidance, with confirmation of correct catheter tip position at the time of insertion. All TVCs were removed as soon as the AVF was deemed successful.

**Outcomes**

The primary outcome was successful AVF function (defined as the successful cannulation with two needles for ≥50% of hemodialysis sessions over a 2-week period), assessed at 6 and 12 months after initial creation. The target blood flow rate was ≥250 ml/min in the initial period of AVF use. The secondary outcomes assessed were the time to AVF maturation (defined as days from AVF creation to first successful cannulation with two needles) and the rates of assisted maturation (need for surgical or endovascular intervention before maturation). Data were censored for patients who had not yet started hemodialysis (within the no TVC group), were on another renal replacement modality (peritoneal dialysis), received a kidney transplant, opted for nondialysis conservative care, died before AVF use, recovered from kidney failure, or transferred to another facility outside our hospital network (Figure 1).

**Statistical Analysis**

Statistical analysis was performed using IBM SPSS Statistics v.26 (SPSS, Chicago, IL, USA). Continuous variables were expressed as mean (and SD) or median (and interquartile range) on the basis of data distribution. Pearson’s chi-squared test was used to compare categorical variables, and Mann–Whitney U test for comparing nonparametric continuous variables. Stepwise backward conditional logistical regression analysis was used to account for the effect of confounding factors. Kaplan–Meier survival curves were generated to determine time to AVF maturation. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated. Type 1 error level was set to P values with a cutoff of <0.05 considered statistically significant.

**Results**

**Patient Characteristics**

Demographic variables (age, sex) and comorbidities (diabetes, hypertension, hypercholesterolemia, and smoking) did not differ between the no TVC and TVC groups, and between the contralateral and ipsilateral TVC groups (Table 1). There were fewer upper-arm (brachiocephalic or brachiobasilic) AVFs in the no TVC group, compared with the TVC group (16% versus 30%, P=0.002), but contralateral and ipsilateral TVC group had similar rates of upper-arm AVF. The contralateral TVC group had fewer right upper-limb AVFs (5% versus 83%; P<0.001) and fewer left-sided TVCs (5% versus 18%; P=0.02) than the ipsilateral TVC group. The median time from TVC insertion to AVF creation was longer in the ipsilateral TVC group (192 days) compared with the contralateral TVC group (139 days), although this difference was not statistically significant (P=0.37).

**Primary Outcomes**

The no TVC group had superior AVF function compared with the TVC group at both 6 (69% versus 54%; OR, 1.84; 95% CI, 1.00 to 3.39, P=0.05) and 12 months (84% versus 64%; OR, 3.10; 95% CI, 1.53 to 6.26, P=0.002). This association remained significant after adjusting for age, sex, diabetes, hypertension, and hypercholesterolemia (Table 2).

The contralateral TVC group had superior AVF function compared with the ipsilateral TVC group at 6 months (60% versus 40%; OR, 2.21; 95% CI, 1.01 to 4.88, P=0.05), but not at 12 months (66% versus 58%, OR, 1.42; 95% CI, 0.62 to 3.25, P=0.40). Using a stepwise backward logistic regression analysis, there was no effect of age, sex, diabetes,
hypertension, hypercholesterolemia, and proportion of left-sided TVCs on AVF function at either 6 or 12 months. However, a longer time interval between TVC insertion and AVF creation was associated with poorer AVF function at both 6 ($P<0.001$) and 12 months ($P=0.01$).

**Secondary Outcomes**

The median time to AVF maturation was longer in the ipsilateral TVC group compared with the contralateral TVC group, although this was not statistically significant (146 versus 121.5 days, $P=0.07$) (Table 3). The time to maturation over 12 months after initial AVF creation for each group is shown as Kaplan–Meier 1-survival curve in Figure 2.

Intervention rates for assisted maturation were lower in the no TVC group compared with the TVC group (12% versus 28%; OR, 0.36; 95% CI, 0.17 to 0.76, $P=0.007$) but similar between the contralateral and ipsilateral TVC groups (29% versus 26%; OR, 1.16; 95% CI, 0.48 to 2.81, $P=0.74$) (Table 3). Interventions performed were fistuloplasty + stent ($n=48$), surgical revision of AVF ($n=6$), and ligation of collateral veins ($n=6$). There were no documented interventions for central venous stenosis.
In this single-center, retrospective, observational cohort study of 287 patients on hemodialysis who had their first upper-limb AVF creation, patients without prior TVC had higher successful AVF use assessed at both 6 and 12 months compared with patients with a previously inserted TVC. The presence of a previous TVC ipsilateral to the AVF was associated with lower successful AVF use at 6 months, but not at 12 months.

Although AVFs are the optimum choice for long-term vascular access, the majority of patients with ESKD start hemodialysis using temporary dialysis catheters. In 2018, 58% of Australian patients started hemodialysis via central venous catheters, compared with 42% with an AVF or arteriovenous graft (11). Dialysis catheter use has been associated with increased morbidity and mortality (12) and minimizing their use has been a challenge in the care of patients on dialysis. However, the utility of AVFs depends on their successful maturation and function, and primary failure of AVFs remains a major limiting factor. In one study of patients on prevalent dialysis in the United States, AVF non-use was noted in 36% of patients, and among those

### Table 1. Demographic and clinical characteristics of patients at baseline

| Characteristics                      | No Tunneled Vascular Catheter (n=145) | Tunneled Vascular Catheter (n=142) | P Value | Contralateral Tunneled Vascular Catheter (n=102) | P Value | Ipsilateral Tunneled Vascular Catheter (n=40) | P Value |
|--------------------------------------|---------------------------------------|-------------------------------------|---------|-----------------------------------------------|---------|-----------------------------------------------|---------|
| Demographics                         |                                       |                                     |         |                                               |         |                                               |         |
| Age, yr, median (interquartile range) |                                       |                                     | 0.25    |                                               |         |                                               | 0.27    |
| Female sex, n (%)                    |                                       |                                     | 0.69    |                                               |         |                                               | 0.29    |
| Comorbidities, n (%)                 |                                       |                                     | 0.89    |                                               |         |                                               | 0.54    |
| Diabetes                             |                                       |                                     | 0.90    |                                               |         |                                               | 0.45    |
| Hypertension                         |                                       |                                     | 0.90    |                                               |         |                                               | 0.45    |
| Hypercholesterolemia                 |                                       |                                     | 0.76    |                                               |         |                                               | 0.26    |
| Smoking                              |                                       |                                     | 0.76    |                                               |         |                                               | 0.26    |
| Cause of ESKD, n (%)                 |                                       |                                     | 0.76    |                                               |         |                                               | 0.26    |
| Diabetes                             |                                       |                                     | 0.76    |                                               |         |                                               | 0.26    |
| Glomerulonephritis                   |                                       |                                     | 0.76    |                                               |         |                                               | 0.26    |
| Hypertension                         |                                       |                                     | 0.76    |                                               |         |                                               | 0.26    |
| Hypercholesterolemia                 |                                       |                                     | 0.76    |                                               |         |                                               | 0.26    |
| Smoking                              |                                       |                                     | 0.76    |                                               |         |                                               | 0.26    |
| TVC insertion to AVF creation, d, median (interquartile range) | n/a                                   |                                     | 0.76    |                                               |         |                                               | 0.26    |
| Left-sided TVCs, n (%)               |                                       |                                     | 0.76    |                                               |         |                                               | 0.26    |
| AVF location, n (%)                  |                                       |                                     | 0.76    |                                               |         |                                               | 0.26    |

AVF, arteriovenous fistula; TVC, tunneled vascular catheter; n/a, not available.

### Table 2. Primary outcomes

| AVF function, months, n (%) | No Tunneled Vascular Catheter | Tunneled Vascular Catheter | Odds Ratio | 95% Confidence Interval | P Value |
|-----------------------------|-------------------------------|----------------------------|------------|--------------------------|---------|
| 6                           | 48 out of 70 (68.6)           | 70 out of 129 (54.3)       | 1.84       | 1.00 to 3.39             | 0.05    |
| 12                          | 70 out of 83 (84.3)           | 73 out of 115 (63.5)       | 3.10       | 1.53 to 6.26             | 0.002   |

| Contralateral TVC | Ipsilaterial TVC | Odds Ratio | 95% Confidence Interval | P Value |
|-------------------|-----------------|------------|-------------------------|---------|
| 6                 | 56 out of 94 (59.6) | 14 out of 35 (40.0) | 2.21       | 1.01 to 4.88 | 0.05 |
| 12                | 54 out of 82 (65.9) | 19 out of 33 (57.6) | 1.42       | 0.62 to 3.25 | 0.40 |

AVF, arteriovenous fistula; TVC, tunneled vascular catheter.

*a*Backward conditional logistical regression applied to adjust for baseline variables (age, sex, diabetes, hypertension, and hypercholesterolemia).

*b*Backward conditional logistical regression applied to adjust for baseline variables, days from TVC insertion to AVF creation, and left-sided TVC.
AVFs that were successfully used, only about half were used within the first 4 months after creation (13). Older age, female sex, Black race, and comorbid conditions (cardiovascular disease, peripheral vascular disease, and diabetes) were associated with increased primary AVF failure.

There is no uniform agreement in the literature on how to define AVF function and maturation, leading to a heterogeneous mix of studies that are difficult to compare (14). Our definition of function (successful cannulation using two needles for ≥50% sessions over a 2-week period) was chosen on the basis of its practical nature and clinical relevance to patient management. We use this criterion in our center to deem an AVF successful and guide the decision for removal of the concurrent TVC.

Few retrospective studies have noted that presence of a long-term dialysis catheter at the time of AVF creation is associated both with lower successful AVF use (13) and increased long-term AVF failure (5). It is unclear if existing TVCs have a direct effect on the successful maturation and/or long-term survival of subsequent AVFs. Successful maturation of an AVF depends on increased flow through the vein, with the resultant shear stress causing remodeling and arterialization of the vein (15). Central vein stenosis could potentially delay maturation of subsequent AVFs by compromising blood flow and interfering with AVF remodeling. Central venous stenosis is a well-described complication of long-term dialysis catheters, but its prevalence and clinical outcomes have not been well studied (8). Central vein stenosis is more common in central venous catheters placed in the left internal jugular vein, presumably due to its longer and more tortuous course (16). Imaging of central veins is not routinely performed, and venous stenosis is often diagnosed incidentally, or when there are overt signs or symptoms. In a study of 2811 patients on hemodialysis, central venous stenosis was noted in 4% of patients after a median time of 2.9 years on dialysis (17). It was found that catheter duration, number, and left-sided catheters were associated with higher risk of central venous stenosis (17). The majority (76%) were asymptomatic, with diagnosis made on imaging performed for vascular access or other reasons, suggesting the true prevalence of central venous stenosis is likely to be higher. In our study, the presence of a previous TVC was associated with lower successful AVF use at 6 and 12 months, compared with AVF with no previous TVC. This effect was noted independently of patient characteristics (such as age, sex, hypertension, and diabetes), perhaps suggesting catheter-related factors could be responsible. No patient in our study had endovascular or surgical intervention for central venous stenosis, but subclinical central venous stenosis could have been a contributing factor. Many patients in the no TVC group were excluded from analysis at 6 and 12 months (46 and 30 patients, respectively), because they had not yet started dialysis at these time points. It is possible the decision to initiate dialysis treatment in this group may be influenced by the maturation (or the lack of) of AVF, which can contribute to a clinical bias favoring this group.

A significant proportion of central venous stenosis occur in the brachiocephalic vein ipsilateral to the TVC insertion site (17), which could potentially affect function of subsequent AVFs created on the same side. A previous retrospective study of 132 central venoplasties in 76 patients noted that ipsilateral TVCs were present in 58% of patients, and they were associated with poorer assisted patency rates (18). In our study, the ipsilateral TVC group had lower successful AVF use at 6 months, but not at 12

### Table 3. Secondary outcomes

|                | Contralateral Tunneled Vascular Catheter | Ipsilateral Tunneled Vascular Catheter | Odds Ratio | 95% Confidence Interval | P Value |
|----------------|-----------------------------------------|---------------------------------------|------------|-------------------------|---------|
| Time to AVF maturation, days, median (interquartile range) | 121.5 (94) | 146 (97) | 0.07 |                       |         |
| No TVC         |                                        |                                       |            |                         |         |
| Assisted maturation, n (%) | 11 out of 89 (12.4) | 36 out of 129 (27.9) | 0.36 | 0.17 to 0.76 | 0.007 |
| TVC            |                                       |                                       |            |                         |         |
| Assisted maturation, n (%) | 27 out of 94 (28.7) | 9 out of 35 (25.7) | 1.16 | 0.48 to 2.81 | 0.74 |

AVF, arteriovenous fistula; TVC, tunneled vascular catheter.
months, and this effect was independent of baseline characteristics (age, sex, diabetes, hypertension, and hypercholesterolemia). We noted a higher proportion of left-sided TVCs in the ipsilateral TVC group (18% vs 5%), although this did not affect the primary outcome at 6 or 12 months in the multivariate analysis. Instead, a longer interval between TVC insertion and AVF creation was associated with a reduced likelihood of successful AVF function at both 6 and 12 months. This may be an important confounding variable in the assessment of our primary outcome, because a longer duration of dialysis catheter use has been shown to increase the risk of central venous stenosis (17).

The median time to successful AVF use in the ipsilateral TVC group was also longer compared with the contralateral TVC group (145 vs 121.5 days), although this did not reach statistical significance. The finding of lower successful AVF function in the ipsilateral TVC group at 6 months, but not at 12 months, suggests the time to successful AVF use may be delayed in the ipsilateral TVC group. We believe the difference in clinical AVF outcomes at 6 and 12 months is likely due to primary failure or delayed maturation of the AVF. Only a small number of patients (n=4) were observed to have secondary failure of a previously mature and successfully used AVF within the 12-month study period.

Other studies have also evaluated the effect of previous TVC location on AVF maturation and long-term outcomes. In one previous retrospective study of 322 patients, it was noted that AVF survival was lower in those with ipsilateral TVCs compared with contralateral TVCs, but the primary AVF failure rates were similar (50% vs 53%, P=0.70) (19). In another retrospective study involving 201 patients, the rate of cannulation failure was higher in AVFs that had ipsilateral TVCs (39% vs 11%, P<0.001), whereas the overall AVF survival was longer in the contralateral TVC group (778.7 vs 247.3 days, P<0.002) (9). A third retrospective study of 187 patients, however, showed no difference in assisted (74% vs 64%, P=0.22) and unassisted (62% vs 55%, P=0.41) functional AVF maturation between ipsilateral and contralateral TVC groups (20). Of note, this study was on a veterans population, which was predominantly male (>90%) and has been associated with better AVF outcomes (13).

In our study, the rates of assisted maturation (endovascular or surgical intervention before first AVF use) were lower in the no TVC group compared with the TVC group (12% vs 28%, P=0.007), but similar between the contralateral and ipsilateral TVC groups (29% vs 26%, P=0.74). A retrospective national dialysis cohort study of 7301 US patients noted that 46% of AVFs needed assisted maturation, with higher subsequent intervention rates postmaturation, and ultimately lower long-term AVF survival in those needing greater than or equal to four interventions prematuration (10). By comparison, we noted an overall lower rate of interventions for assisted maturation in our study population. Although early endovascular interventions increase the pool of usable AVFs through assisted maturation, it is unclear if the procedure itself can lead to increased subsequent AVF failure. Endothelial injury and restenosis at the site of intervention may be potential contributing factors (21).

We do note the median time to first successful use of AVF in our cohort of patients on dialysis was longer than previously reported in literature. In the 2018 international Dialysis Outcomes and Practice Patterns comparison study, it was reported to range from 10 days in Japan, 46 days in Europe/ANZ, and 82 days in the United States (22). Our patient demographics and comorbidities are not different to what is reported in the literature, so other factors such as patient adherence to surgical follow-up, frequency of AVF imaging postcreation, lower rates of intervention for assisted maturation, and local surgical practices may be contributing to the delayed AVF use in our study cohort.

Our study does have several limitations. As a single-center, retrospective, observational cohort study, these findings are largely associations and do not imply a causal relationship between previous catheter use and location and subsequent AVF function. The 6- and 12-month time points chosen for our primary outcome were not on the basis of any previously reported outcome studies, but do provide an opportunity to assess early AVF function, which in turn could predict long-term survival of AVF, although these longer-term outcomes were not specifically assessed in this study. We acknowledge that the small sample size in this study could have resulted in a type 2 error, leading to the loss of statistical significance at 12 months when comparing the ipsilateral and contralateral TVC groups. Finally, the analysis of the nil TVC group is challenging, given a large proportion of patients were excluded at outcome analysis as they had not yet started hemodialysis treatment.

In this single-center, retrospective, observational cohort study, the presence of an existing TVC at the time of AVF creation was associated with lower rates of successful AVF function in those needing hemodialysis at 6 and 12 months and increased rates of intervention for assisted maturation. The presence of ipsilateral TVC was associated with lower rates of AVF function at 6 months, but not at 12 months. The time to AVF use was longer in the ipsilateral TVC group compared with the contralateral TVC group, although this was not statistically significant. In patients being considered for AVF creation, the location of existing or previous TVCs should be additional considerations in planning surgery to optimize AVF outcomes.

Disclosures

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Author Contributions

A. Makris, G. Narayanan, and J. Wong conceptualized the study; A. Aravindan, I. De Guzman, J. Diep, H. Nandakoban, and J. Wong were responsible for the data curation; J. Diep, A. Makris, and G. Narayanan were responsible for the formal analysis; G. Narayanan was responsible for the methodology; A. Makris and
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