

The Effect of Risk of Maturation Failure and Access Type on Arteriovenous Access-Related Costs among Hemodialysis Patients

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Abstract

Background Several studies report lower costs associated with attaining and maintaining patency for arteriovenous (AV) fistulas as compared to AV grafts among patients receiving hemodialysis. However, these costs may vary according to the AV access's risk of failure to mature (FTM). The aim of this study was to examine the effect of AV access type and risk of FTM on the total costs of attaining and maintaining AV access patency over 1, 3, and 5 years postcreation, among incident accesses.

Methods All first AV access creations (January 1, 2002–January 1, 2018), revisions/resections, and interventions from a single academic institution were prospectively captured. The units costs (from 2011 in CA\$) were estimated primarily through the provincial patient Ontario Case Costing Initiative database. The present value of total vascular access-related costs from a third-party payer perspective was calculated by multiplying specific unit costs by the number of AV access creations, revisions/resections, and interventions from the date of creation to 1, 3, and 5 years post creation. The potential associations of AV access type and FTM risk stratum with AV access cost were examined using log-linear models and generalized estimating equations.

Results A total of 906 patients were included in the study, of which 696 had fistulas and 210 had grafts. The median present value of total costs to attain and maintain AV access over 1, 3, and 5 years was positively associated with the highest FTM risk stratum in all models. It was not associated with AV access type when the interaction between AV access type and FTM risk stratum was considered.

Conclusions The costs of attaining and maintaining AV access were increased among patients with high/very high FTM risk. Risk of FTM, related interventions, and costs should be considered when choosing vascular access type for an individual patient.

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Introduction

For adequate hemodialysis, a reliable vascular access is essential and remains the “Achilles heel” of hemodialysis. The United States national quality initiative to improve vascular access outcomes, originally called “Fistula First,” was based on the perception that arteriovenous (AV) fistulas have superior patency, the fewest complications, and are less costly compared with other vascular access types (1,2). Indeed, central venous catheters (CVC) have been established as being associated with the highest rates of complications, particularly infection (3–10), although they are often needed as a temporary measure, such as until an AV access (fistula or graft) can be created and used, or as a valid long-term option in select circumstances (11,12). The validity of Fistula First has recently been challenged in comparisons of outcomes of fistulas and grafts (12–16).

A systematic review of observational studies comparing clinical outcomes between fistulas and grafts

found that the former is associated with high rates of maturation failure but longer-term patency, whereas the latter is more likely to mature and mature quickly, but with shorter patency (17). The review noted that the included studies are subject to significant risk of bias (17), particularly in the form of selection bias from several sources: (1) patients in whom grafts were placed may have not been eligible for a fistula, because fistulas are generally not created in patients with a shorter life expectancy or significant heart failure (18); (2) patients in whom grafts are placed may have needed a more urgent start on dialysis and therefore may be at greater risk for complications (19); and (3) most of these studies are not analyzed according to the intention-to-treat principle, in other words, they are analyzed by the created and/or used access rather than the intended access (20).

There are limited studies that detail the costs associated with attaining and maintaining patency of AV access among incident and prevalent patients. (12,21–25).

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These studies demonstrate that significant resources, including diagnostic and interventional radiology and surgical revisions, are required to facilitate and maintain AV access patency. In this study, we build on the work of Manns *et al.* (21) by capturing the costs associated with both attaining and maintaining patency for fistulas and grafts. However, unlike previous studies that generally conducted an undifferentiated comparison of fistula and graft cost comparison, we will also adjust for the risk of fistula maturation failure using the failure-to-mature (FTM) risk score (24,25) and the interaction of the FTM risk score with AV access type. The FTM risk score has been previously validated and considers several factors in its computation of risk (*i.e.*, age, peripheral vascular disease [PVD], coronary artery disease, and ethnicity). The goal of this study is to analyze the effect of AV access type and FTM risk on the total costs of attaining and maintaining patency of AV access over 1, 3, and 5 years post creation, among incident patients needing hemodialysis.

The specific objectives of this study are to: (1) compare the rates and proportions of AV access creations, revisions, removals, and other interventions among fistulas and grafts; (2) describe the total AV access-related costs from a third-party payer perspective at 1, 3, and 5 years postcreation among fistulas and grafts; and (3) examine whether the total AV access-related costs were associated with AV access type and their FTM risk stratum as determined by their FTM risk score.

Materials and Methods

Population

The Toronto General Hospital - University Health Network (TGH-UHN) is a large academic based institution in Toronto, Ontario, Canada, that serves 250–350 patients in its in-center hemodialysis program. Patients with a first AV access created from January 1, 2002 to January 1, 2018 at TGH-UHN were included in this study. The patient could have been predialysis or have already started hemodialysis with a CVC (see clinical data collection below for details). This study was approved by the UHN research ethics review board.

Clinical Data Collection

At TGH-UHN, a hemodialysis vascular access clinical and research database (VASPRO) is maintained that prospectively captures key patient characteristics, the date of all vascular access creations, removals, related endovascular and surgical interventions at TGH-UHN (any care occurring elsewhere is not captured), and the reasons for vascular access failure. This database collects data as long as the patient is a patient in the hemodialysis program at TGH and also captures reasons for leaving the program (*e.g.*, change of modality, death). The first day of costing was the day of surgical creation of the AV access. For the duration of the AV access, all AV access history including date of AV access creation and subsequent interventions required to facilitate and/or maintain patency (*i.e.*, angiograms, angioplasties, thrombolysis, revisions), date of access termination, reason for access termination, and CVC use are captured.

For the purposes of this study, data on all patients needing hemodialysis who had a vascular access created from January 1, 2002 to January 1, 2018 were retrieved from

VASPRO. The patients' primary access during the study period was selected so that there was only one access captured per patient, ensuring independence of the unit of analysis. Specifically, sociodemographic data collected at the time of access creation including age and ethnicity, CKD etiology, and comorbidities were extracted (see Table 1 for full list of baseline characteristics). For the duration of the AV access, all AV access history including date of AV access creation and subsequent interventions required to facilitate and/or maintain patency (*i.e.*, angiograms, angioplasties, thrombolysis, revisions), date of access termination, reason for AV access termination, and CVC use were retrieved.

For the analyses related to access days and access-related interventions, the cohort of patients included all primary AV access during the study period and all retrieved data from the surgical creation of the AV access to the termination of the primary access or the end of the study period.

For the cost analyses, three cohorts of patients were included. Only those patients for whom there was complete follow-up data (*i.e.*, their access had not been terminated, or the study period had not ended) at 1, 3, and 5 years post-creation were included in the analysis for each time point, respectively, with the first day of costing being the day of

Table 1. Baseline characteristics of all primary permanent accesses (n=906)

| Characteristics | Access Type, Count (%) | |
|---------------------------|------------------------|---------------|
| | Fistula (N=696) | Graft (N=210) |
| Age | | |
| <65 yr | 461 (66%) | 130 (62%) |
| ≥65 yr | 235 (34%) | 80 (38%) |
| Ethnicity | | |
| White | 380 (55%) | 117 (56%) |
| Other | 316 (45%) | 126 (44%) |
| Etiology of ESKD | | |
| Hypertension | 66 (10%) | 16 (8%) |
| Diabetes | 130 (19%) | 48 (23%) |
| GN | 122 (18%) | 28 (13%) |
| Interstitial nephritis | 4 (0.6%) | 6 (3%) |
| Other ^a | 169 (24%) | 45 (21%) |
| Comorbidities | | |
| CHF | 52 (8%) | 20 (10%) |
| COPD | 38 (6%) | 12 (6%) |
| Diabetes mellitus | 199 (29%) | 76 (36%) |
| CAD | 122 (18%) | 41 (20%) |
| Hypertension | 412 (59%) | 136 (65%) |
| PVD | 53 (8%) | 17 (8%) |
| Other ^b | 324 (47%) | 94 (45%) |
| Risk stratum ^c | | |
| Low | 197 (28%) | 50 (24%) |
| Moderate | 318 (46%) | 103 (49%) |
| High | 139 (20%) | 45 (21%) |
| Very high | 42 (6%) | 12 (6%) |

CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; PVD, peripheral vascular disease.

^a*E.g.*, combination diabetes and hypertension, polycystic kidney disease and other genetic, ischemic, and toxic injuries.

^b*E.g.*, cancer, amyloidosis, liver cirrhosis, and other gastrointestinal disorders.

^cCalculated based on failure-to-mature prediction score=3+2(age)+3(PVD)+2.5(CAD)–3(white).

surgical creation of the AV access. This prevents potential bias associated with comparing accesses with differing longevity, because accesses with a shorter observation period would potentially accumulate less costs, as was observed in the study by Manns *et al.* (21).

Quantifying the CVC use while the AV access was *in situ* included computing based on the start and end date of all CVCs: (1) the number of CVC insertions during, (2) the number and date of CVC removals, and (3) the number of CVC days from the date of AV access creation to AV access removal. The burden of CVC-related complications during the lifetime of the AV access were then computed by drawing on rates per 1000 days from clinical trials previously conducted at TGH-UHN and included bacteremia (0.383) (26), exit-site infections (0.595) (26), malfunctions requiring tissue plasminogen activator (tPA) use (3.3) (27), and hospitalizations (0.28) (27).

Any secondary AV access creation/use was not included so as to focus this analysis on primary AV access-related cost, the population in which the FTM risk score was developed.

The costs of bacteremia related to AV accesses were not included in this analysis because these were not consistently captured in the VASPRO database. However, a recent large prospective study in 177,875 prevalent and 11,290 incident patients receiving hemodialysis found no difference in vascular access infection rates between patients with a graft or fistula among both incident and prevalent patients, and the rate of infection with both types of access was very low (28).

Estimating Unit Costs

To obtain an estimate of the unit costs of vascular access-related events and complications, five separate sources were used: (1) aggregated estimated costs from the Ontario Case Costing Initiative (OCCI) database, (2) UHN interventional radiology and surgery department costing records, (3) UHN Pharmacy cost records, (4) UHN ward costs, and (5) previous costing study in tPA use (29). These sources are discussed further below:

1. The OCCI is an undertaking of the Ontario Ministry of Health and Long-Term Care; its primary objective is to collect case-costing data in support of improved management decision making and resource allocation. OCCI collects case-cost data for acute inpatient, day surgery, and ambulatory care cases, as well as complex continuing care, rehabilitation, mental health, and community care centers' cases (30). The OCCI makes aggregate data for the province of Ontario publicly available using the online costing analysis tool. In this study, the median total costs, direct costs, and indirect costs in Ontario for 2011 were obtained by entering the procedural codes for each type of vascular access-related complication or event into the cost analysis tool, because this is the last year for which the costs were publicly available.
2. TGH-UHN interventional radiology and surgery department records were used to obtain an itemized cost estimate of CVC removal and new CVC insertion, which includes the costs of the CVC, use of the interventional room, and equipment required.
3. TGH-UHN pharmacy cost records were used to obtain an estimate of the cost associated with the outpatient management of CVC-related bacteremia.
4. TGH-UHN costing records were used to estimate the cost per day on the ward to obtain an estimate of the cost of hospitalizations for CVC-associated complications (including infection).
5. We obtained a point estimate for the use of a rescue thrombolytic, recombinant tPA, for CVC malfunction from a cost analysis of the prevention of dialysis CVC malfunction with recombinant tPA (PRECLOT) study (29).

Analysis

Baseline Characteristics. Descriptive statistics were calculated for all baseline characteristics including sex, age, ethnicity, etiology of ESKD, and comorbidities. Patient ethnicity, age, cardiovascular, and PVD statuses were used to determine each patient's risk of fistula maturation failure according to the FTM risk score (25) as low (24%), moderate (34%), high (50%), or very high (69%).

Access Days and Access-Related Interventions. The mean number of AV access days was calculated based on the number of days the access was *in situ*, that is, from the creation date to the access end date of the patients' primary AV access during the study period. Rates (events per 1000 access days) of AV access-related interventions were calculated based on the number of AV access-related interventions during the time the AV access was *in situ*. The rates of CVC-related interventions were calculated by determining the number of CVC days while each AV access was *in situ*. The proportions and rates (events per 1000 access days) of fistulas versus grafts requiring angioplasties, angiograms, thrombolysis, revisions, CVC placements, and having an infection (CVC related) were compared using the Fisher exact test and exact Poisson method, respectively. The mean number of access days, both AV access and CVC days while the AV access was *in situ*, were compared between fistula and grafts using independent samples *t* tests.

Cost Analyses. This study took the perspective of the health care purchaser and includes only direct health care-related costs. Societal costs (*e.g.*, time costs for patients and relatives, patient transport costs), although important to consider, were not captured in VASPRO and therefore were not included. The total costs reported in 2011 in Canadian dollars at 1, 3, and 5 years postaccess creation were calculated by multiplying the unit cost for each intervention by the number of complications requiring intervention from creation to 1, 3, and 5 years postcreation. To take into account time preference, we used discounting to calculate the present value at a rate of 3% per annum (31). Median costs were reported by access type.

The potential association of year of access creation, AV access type and FTM risk stratum with access-related cost was compared at 1, 3, and 5 years using log-linear models and access type and FTM risk with access-related cost over time using generalized estimating equations. Both the main effects of AV access type and FTM risk stratum on costs as well as the main effects and interaction of AV access type and FTM risk stratum were reported. Due to small cell counts in the very high risk stratum, the patients were

collapsed in with high risk for these analyses. All analyses were conducted using SPSS 22.

Results

There were 1343 primary AV accesses created and captured in VASPRO from January 1, 2002 to January 31, 2018, of whom 437 were excluded for this study because they were not in-center TGH-UHN patients (received dialysis at other centers). Of the 906 remaining accesses, 662 were *in situ* for a minimum of 1 year, 419 were *in situ* for a minimum of 3 years, and 275 were *in situ* for a minimum of 5 years. The mean number of access days (length of follow-up) for fistulas was 1539.2 and 1038.5 for grafts.

Baseline Characteristics by Vascular Access Type

A total of 906 patients were included in the study, of which 696 had fistulas and 210 had grafts (see Figure 1 for AV access type by year). The characteristics used to calculate the risk score (listed in Table 1) for patients with fistulas and grafts included being aged ≥ 65 years (34% versus 38%, respectively), being white (55% versus 56%, respectively), having coronary artery disease (18% versus 20%, respectively), and having PVD (8% versus 8%, respectively). When stratified by risk of failure, among fistulas 28% were classified as low risk, 46% were medium risk, 20% were high risk, and 6% were very high risk. Among grafts, 24% were classified as low risk, 49% were medium risk, 21% were high risk, and 6% were very high risk.

Vascular Access-Related Interventions over the Access Lifetime

The proportion of fistulas requiring radiologic imaging was higher than that of grafts: angiogram (14% for fistulas versus 8% for grafts, $P=0.03$). The proportion of fistulas requiring endovascular interventions to promote or maintain

patency was generally lower than that of grafts including angioplasty (34% for fistulas versus 42% for grafts, $P=0.05$) and thrombolysis (8% for fistulas versus 34% for grafts, $P<0.001$). The insertion of a new CVC during the AV access's lifetime was higher in fistulas than grafts (22% for fistulas versus 14% for grafts, $P=0.01$) (Table 2). Similar trends were reflected in the rate (frequency) of events over the AV access lifetime span (events per 1000 access days; see Table 2).

Median Vascular Access-Related Costs

For unit cost estimates see Table 3. The median vascular access-related costs, undifferentiated by FTM risk, were lower for fistulas than grafts at 1 year (\$3822.21 for fistulas versus \$4172.34 for grafts; see Figure 2), 3 years (\$4765.22 versus \$7953.31; see Figure 3), and 5 years (\$5856.21 versus \$8324.39; see Figure 4) postcreation.

Impact of FTM Risk Score and Access Type on Vascular Access-Related Costs

The potential association of AV access type, FTM risk stratum, and year of AV access creation with access-related cost was examined at 1, 3, and 5 years, as well as AV access type and FTM risk stratum with access-related cost over time. The highest risk stratum and decreasing year of AV access creation was consistently associated with higher cost in all models at all time points. However, AV access type was not significantly associated with higher cost in any of the models that considered the interaction between AV access type and risk stratum (Table 4).

Discussion

The main finding of this study is that the costs of attaining and maintaining AV access patency increased with increasing risk of fistula maturation failure at 1, 3, and 5 years. Those AV accesses that were likely to be at high risk of

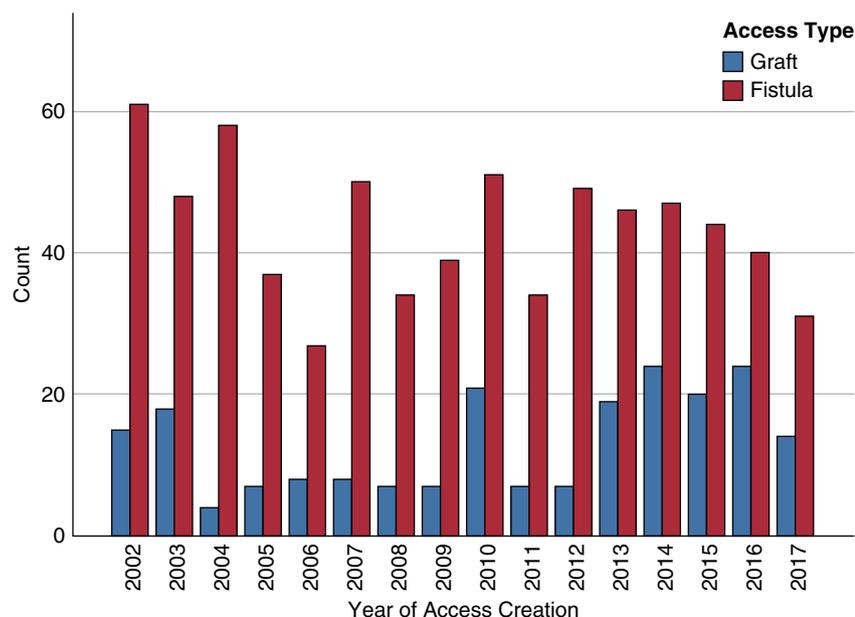


Figure 1. | Decreasing numbers of fistulas and increasing numbers of grafts created during the study period ($n=906$).

Table 2. All primary accesses—comparing proportions and rates of accesses requiring interventions (n=906)

| Access Lifetime Intervention | Vascular Access Type | | | | Comparison | |
|------------------------------|-------------------------------------|-------|-------------------------------------|-------|------------------------------|----------------------|
| | Fistula (n=696) | | Graft (n=210) | | % Difference (95% CI) | P Value ^b |
| | Proportions | | Proportions | | | |
| | n (%) ^a | | n (%) ^a | | | |
| Angioplasty | 239 | (34%) | 88 | (42%) | 8% (0.19% to 15%) | 0.05 |
| Angiogram | 95 | (14%) | 17 | (8%) | 6% (0.44% to 10%) | 0.03 |
| Thrombolysis | 56 | (8%) | 72 | (34%) | 26% (20% to 33%) | <0.001 |
| Revisions | 58 | (8%) | 11 | (5%) | 3% (-1% to 6%) | 0.14 |
| CVC insertion | 154 | (22%) | 30 | (14%) | 8% (2% to 13%) | 0.01 |
| CVC removal | 236 | (34%) | 79 | (38%) | 4% (-4% to 11%) | 0.34 |
| CVC use ^c | 398 | (57%) | 112 | (53%) | 4% (-4% to 12%) | 0.32 |
| Rates | n ^d Per 1000 Access Days | | n ^d Per 1000 Access Days | | Incident Rate Ratio (95% CI) | P Value ^e |
| Angioplasty | 684 | 0.64 | 345 | 1.58 | 0.40 (0.0020 to 81.69) | <0.001 |
| Angiogram | 127 | 0.12 | 20 | 0.09 | 1.29 (1.07 to 1.49) | 0.29 |
| Thrombolysis | 79 | 0.07 | 174 | 0.80 | 0.09 (0.00019 to 45.32) | <0.001 |
| Fistula or graft revisions | 58 | 0.05 | 11 | 0.05 | 1.07 (21.19 to 0.051) | 0.83 |
| New CVC insertion | 207 | 0.19 | 36 | 0.17 | 1.17 (1.4941 to 0.8967) | 0.38 |
| CVC removal | 263 | 0.25 | 86 | 0.39 | 0.62 (0.042 to 9.27) | <0.001 |
| Access length | Mean | | Mean | | Mean Difference (95% CI) | P Value ^f |
| AV access days | 1539.21 | | 1038.53 | | 500.67 (289.40 to 711.94) | <0.001 |
| CVC days | 214.74 | | 145.40 | | 69.34 (12.10 to 126.58) | 0.02 |

CVC, central venous catheter; AV, arteriovenous.

^an is the number of accesses and % is the proportion of accesses with at least one intervention during the access lifetime.

^bProportions compared using chi-squared test.

^cHad a CVC *in situ* any time during the access lifetime.

^dn is the total number of procedures performed in all accesses of that type.

^eRates compared using the Fisher exact test.

^fMeans compared using independent samples *t* test.

failure also had the greatest need for interventions and consequent increased costs to achieve and maintain access patency, which is consistent with other studies (12,33–35). However, AV access type was not a significant predictor of cost when the interaction between access type and risk of fistula maturation failure was considered. Year of creation was negatively associated with cost, which suggests that more recent advances in technologies and strategies to inform vascular access placement may have been effective in reducing AV access-related costs over time.

Other previous cost studies have indicated fistulas are less costly compared with grafts (21,22). The primary reason for the difference in findings likely relate to the difference in how costs were compared. Rather than an undifferentiated comparison of fistula and graft cost comparison, we stratified our analyses according to risk of AV access maturation failure. Indeed, we did find that the undifferentiated median cost is lower for fistulas than grafts; however, when we adjusted for FTM risk stratum and AV access type, as well as the interaction, we found that FTM risk stratum was associated with increasing cost and AV access type was not. The differences in the magnitude of the median cost in this study as compared to others may be attributable to the variance in unit cost estimates globally; however, the unit cost estimates in our study generally fall within the range of those in the literature: angiograms from \$90 to \$404 (22,36,37), angioplasties from \$571 to \$1939 (22,36–39), and thrombolysis from \$1381 to \$6802 (37,39–42).

Thus, the findings of this study highlight the need for careful consideration of vascular access choice based on the

patient's risk of fistula maturation failure from not only a clinical but also an economic standpoint. Although fistulas were once thought to be associated with the lowest morbidity and mortality of all types of vascular access, this may be true only if they mature enough to be used to deliver adequate dialysis. If fistulas are created in patients in whom there is likely to be significant difficulties in attaining patency, resulting in greater interventions, CVC use, and their complications (43–45), their main advantage over grafts may be lost. This may be particularly important to consider in subsets of the hemodialysis population such as patients who are elderly, those with diabetes, or female patients, where fistulas and grafts have been shown to have equivalent outcomes (12,46).

This study has potential implications related to policy on hemodialysis vascular access in North America because lower costs are one of the cited reasons for the promotion of fistulas in the Fistula First quality initiative which has been widely adopted (1,2). Given that fistulas tend to have greater rates of maturation failure but better longer-term patency than grafts (12–14,17), costs may vary based on FTM risk. In this study, we found that increasing FTM risk score was associated with increasing cost. When FTM risk is considered in the model, AV access type was not a significant predictor of cost. Therefore, if resource utilization is a concern, both fistulas and grafts should be considered, particularly in those patients for whom maturation failure is highly likely; a graft may be a better choice because recent studies have shown that they have a shorter maturation time (less exposure to a CVC), require less interventions to

Table 3. Unit costs of vascular access surgery from Ontario Case Costing Initiative costing analysis tool (2011)

| Surgery Type | Median in \$ (SD) | | | | | | Point Estimate in \$ ^a |
|--|---------------------|-----|------------------------|-----|----------------------------------|------|-----------------------------------|
| | Total Cost Per Case | | Indirect Cost Per Case | | Total Cost Per Case ^a | | |
| Permanent access-related surgery and interventions | | | | | | | |
| Access creation ^a | 1631 | 719 | 497 | 220 | 2128 | 849 | — |
| Access revision ^a | 1223 | 800 | 464 | 255 | 1687 | 1053 | — |
| Angioplasty ^a | 1954 | 621 | 675 | 221 | 2629 | 841 | — |
| Angiogram ^a | 1346 | 480 | 488 | 139 | 1833 | 617 | — |
| Thrombolysis ^a | 1121 | 785 | 375 | 164 | 1496 | 904 | — |
| CVC-related interventions (CVC use while permanent access <i>in situ</i>) | | | | | | | |
| Outpatient treatment for vascular access-associated bacteremia per event ^b | | | | | | | 262 |
| CVC removal and new insertion ^c | | | | | | | 1121 |
| Cost of hospital per day related to CVC-related complications (non-ICU) (price per day) ^d | | | | | | | 700 |
| Cost of rescue tPA for patients who develop CVC malfunction ^e | | | | | | | 533 |

CVC, central venous catheter; ICU, intensive-care unit; tPA, tissue plasminogen activator; OCCI, Ontario Case Costing Initiative; TGH-UHN, Toronto General Hospital - University Health Network; PRECLOT, prevention of dialysis CVC malfunction with recombinant tissue plasminogen activator.

^aSource: OCCI costing analysis tool (2011), the median total costs obtained from OCCI are derived from the sum of the direct costs (*i.e.*, costs directly related to the provision of patient care, such as nursing in the operating room, diagnostic imaging, pharmacy, and laboratory work required) and the indirect costs (*i.e.*, costs which includes overhead expenses, such as those related to managing relevant facility operations) of all patients receiving hemodialysis who had their vascular access-related complications or events in all OCCI hospitals in Ontario during 2011.

^bSource: UHN Pharmacy costing records, the dose and duration of antibiotic treatment, as well as the cost of laboratory monitoring for the antibiotics were based on the outpatient hemodialysis diagnostic and treatment algorithm as follows. For this study, we assumed that once a catheter-related bacteremia is suspected, two sets of blood cultures, which cost CA\$102 per set, are obtained as per guideline recommendations (32). Empirical parenteral vancomycin and an aminoglycoside, tobramycin, are initiated at three administrations per week, until sensitivities and cultures return. The list price of vancomycin and tobramycin were used; the duration of antibiotic use was estimated to be 2 weeks.

^cSource: TGH-UHN interventional radiology department costing records.

^dSource: TGH-UHN costing records for ward, the cost of hospitalizations for CVC-associated complications were included in this analysis, but not AV access-related complications because these were not consistently captured in our database.

^eSource: PRECLOT study.

attain patency, and offer comparable patency rates (44,45,47,48). Indeed, CVC use was lower among grafts in our study. CVC use, even as a bridge for a maturing AV access, can be associated with complications that put

patients at risk for additional morbidity and mortality and, secondarily, place a heavy drain on health care resources (3–10). CVC-related infections in particular are very costly; estimates of the total direct and indirect costs associated

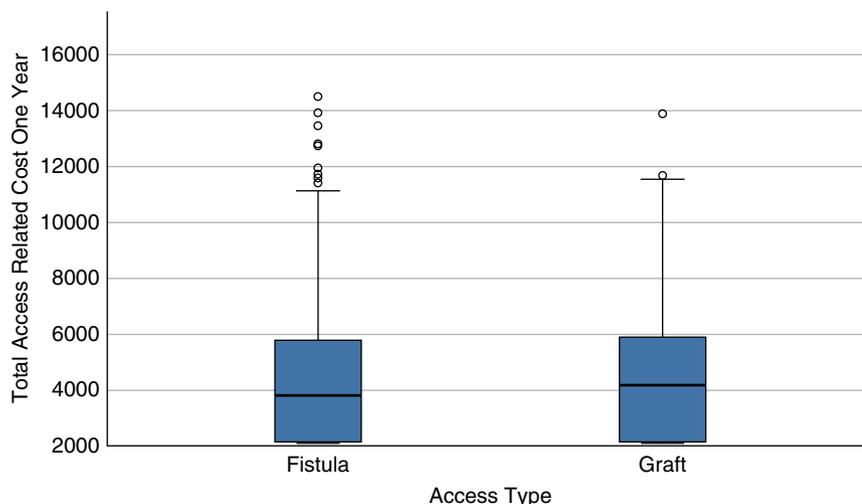


Figure 2. | Simple boxplot showing higher access -related cost at 1 year among fistulas as compared to grafts (comparison unadjusted for FTM risk score) (n=662). Fistula, n=510, median=\$3822.21; graft, n=152, median=\$4172.34.

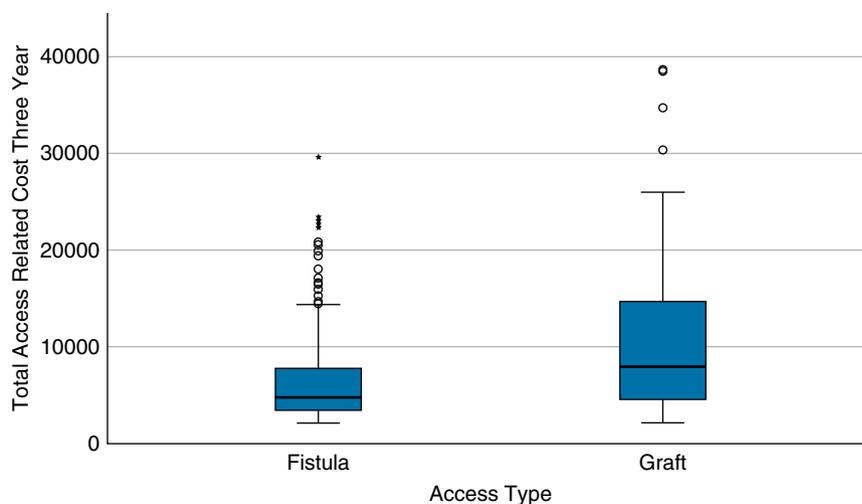


Figure 3. | Simple boxplot showing higher access-related cost at 3 years among fistulas as compared to grafts (comparison unadjusted for FTM risk score) ($n=419$). Fistula, $n=338$, median=\$4765.22; graft, $n=81$, median=\$7953.

with hospitalizations due to CVC-related infection range from US\$17,000 to US\$32,000 (4,8,49,50). In our analysis, we did not include the costs of intensive-care unit stays for patients with CVC-related sepsis, thus underestimating the costs of treating catheter-related infections.

This study has certain limitations that should be noted. Given the cost analysis was conducted at three time points (see analysis below)—1, 3, and 5 years postcreation—only those patients whose AV access was still *in situ* at 1, 3, and 5 years postcreation were included in the analysis at each time point, respectively. Although this prevents potential bias associated with comparing accesses with differing longevity, because accesses with a shorter observation period would potentially accumulate less costs—as was observed in Manns *et al.* study (21), the costs associated with access that failed in less than a year were not captured. Secondly, although our study prospectively followed AV accesses from creation to abandonment and determined their actual

events upon which we calculated the costs, the exact costs accrued for each patient was not used in this study. Rather, we used unit costs and multiplied them by the number of events, yielding a modeled estimate of the cost. Most of the unit costs used for this study represent the cost estimates obtained from the OCCI database, to which a large majority of the hospitals in Ontario, Canada contribute. This province has a single-payer health system and therefore the generalizability of these findings may be limited for areas with different payer models. Thirdly, the number of events was drawn from a single center with multiple surgeons in Toronto, Ontario, Canada, also limiting the generalizability of the findings to other jurisdictions. Fourthly, the FTM risk score was used to compare groups due to its validated ability to predict maturation failure; however, there are other risk factors such as need for an urgent start on dialysis (51) which might be important to adjust for in analyses to minimize the bias in an examination of cost that were not

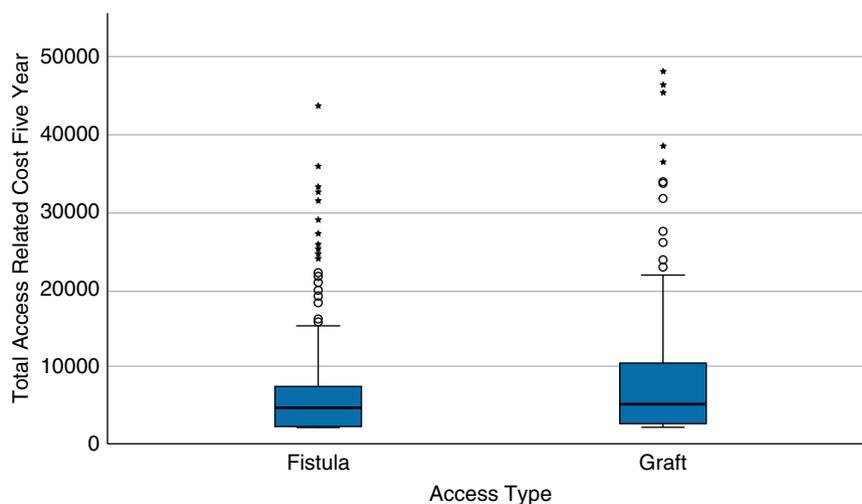


Figure 4. | Simple boxplot showing higher access-related cost at 5 years among fistulas as compared to grafts (comparison unadjusted for FTM risk score) ($n=275$). Fistula, $n=239$, median=\$5856.21; graft, $n=36$, median=\$8324.39.

Table 4. Association of access type and failure-to-mature risk stratum with access-related cost at 1, 3, and 5 yr and over time ($n=662$, $n=419$, $n=275$, $n=275$, respectively)

| Log Cost | Factor | Main Effects | | Main and Interaction Effects | |
|------------------------------------|------------------------------------|--------------------------|---------------------|------------------------------|---------|
| | | Effect Estimate (95% CI) | P Value | Effect Estimate (95% CI) | P Value |
| 1 yr ^a | Year of creation | 0.99 (0.99 to 0.99) | <0.001 | 0.99 (0.99 to 0.99) | <0.001 |
| | High risk ^b | 1.11 (1.06 to 1.16) | <0.001 | 1.19 (1.09 to 1.31) | <0.001 |
| | Moderate risk ^b | 1.02 (0.98 to 1.06) | 0.24 | 1.07 (0.99 to 1.17) | 0.10 |
| | Fistula ^c | 0.96 (0.92 to 1.00) | 0.05 | 1.02 (0.94 to 1.10) | 0.67 |
| | High risk×fistula ^d | | | 0.91 (0.81 to 1.01) | 0.07 |
| 3 yr ^a | Moderate risk×fistula ^d | | | 0.94 (0.85 to 1.04) | 0.22 |
| | Year of creation | 0.98 (0.97 to 0.99) | <0.001 | 0.98 (0.97 to 0.99) | <0.001 |
| | High risk ^b | 1.14 (1.05 to 1.24) | 0.002 | 1.27 (1.06 to 1.52) | 0.01 |
| | Moderate risk ^b | 1.07 (1.01 to 1.14) | 0.04 | 1.15 (0.99 to 1.36) | 0.07 |
| | Fistula ^c | 0.82 (0.76 to 0.88) | <0.001 | 0.89 (0.77 to 1.03) | 0.10 |
| 5 yr ^a | High risk×fistula ^d | | | 0.88 (0.72 to 1.08) | 0.22 |
| | Moderate risk×fistula ^d | | | 0.91 (0.77 to 1.08) | 0.29 |
| | Year of creation | 0.98 (0.97 to 0.99) | <0.001 | 0.98 (0.97 to 0.99) | <0.001 |
| | High risk ^b | 1.22 (1.08 to 1.38) | 0.001 | 1.64 (1.14 to 2.36) | 0.008 |
| | Moderate risk ^b | 1.08 (0.99 to 1.18) | 0.07 | 1.27 (0.98 to 1.66) | 0.07 |
| Over time ^e | Fistula ^c | 0.86 (0.76 to 0.96) | 0.008 | 1.00 (0.79 to 1.27) | 0.99 |
| | High risk×fistula ^d | | | 0.72 (0.49 to 1.06) | 0.09 |
| | Moderate risk×fistula ^d | | | 0.84 (0.63 to 1.11) | 0.21 |
| | 5 yr ^f | 1.24 (1.20 to 1.27) | <0.001 | 1.24 (1.20 to 1.28) | <0.001 |
| | 3 yr ^f | 1.16 (1.13 to 1.19) | <0.001 | 1.16 (1.13 to 1.19) | <0.001 |
| | High risk ^b | 1.14 (1.03 to 1.27) | 0.01 | 1.44 (1.09 to 1.91) | 0.01 |
| | Moderate risk ^b | 1.04 (0.97 to 1.11) | 0.31 | 1.14 (0.93 to 1.39) | 0.21 |
| Fistula ^c | 0.92 (0.84 to 1.02) | 0.10 | 1.02 (0.85 to 1.21) | 0.85 | |
| High risk×fistula ^d | | | 0.77 (0.57 to 1.04) | 0.09 | |
| Moderate risk×fistula ^d | | | 0.90 (0.73 to 1.12) | 0.35 | |

^aLog-linear model.^bReference is low risk.^cReference is graft.^dInteraction term.^eGeneralized estimating equation.^fReference is 1 Year.

considered. It is important to acknowledge that the FTM risk equation was developed before the use of many modern surgical techniques and maturation-assisting procedures and requires further validation in more current samples; however, the finding in this study that the FTM risk equation predicted costs does suggest that the FTM risk equations' predictive value has withstood the test of time when used in populations similar to that in which it was developed. Finally, the outcome of total present value vascular access-related costs from a third-party payer perspective used in these analyses did not consider any patient-related costs such as costs associated with patient transportation for additional vascular access-related interventions (52). Prospective capture of such costs in the long term in future research is critical to more fully capturing all facets of vascular access choice and consequences. Although lower costs are one of the widely cited reasons for the promotion of fistulas (1,2), our study found that this varies based on the risk of fistula maturation failure. Higher present value of total vascular access-related costs was associated with elevated FTM risk scores, but vascular access type was not. Consistent with previous clinical studies (12–14,17), fistulas had higher rates of interventions associated with attaining patency, whereas grafts had higher rates of intervention associated with maintaining patency. Rather than promoting only one type of vascular access, policies related to vascular access should encourage thinking about the

patient's risk of fistula success/failure. Use of the FTM risk score is one aid that can be used in clinical decision making and patient education, but we encourage research to update the FTM risk score to encompass other important variables that affect the success and cost of vascular access creation and use. Indeed, there must be careful consideration of other dimensions including overall health status, life expectancy, support systems, and functional capacity as well as their personal goals and preferences when deciding on what vascular access is optimal for a given patient.

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Author Contributions

S.D. Kosa and C.E. Lok were responsible for formal analysis and wrote the original draft; A. Gafni, S.D. Kosa, C.E. Lok, and L. Thabane were responsible for methodology; A. Gafni, C.E. Lok, and L. Thabane were responsible for supervision; C.E. Lok was responsible for resources; all authors were responsible for conceptualization and edited and reviewed the manuscript.

Disclosures

A. Gafni, S.D. Kosa, C.E. Lok, and L. Thabane have nothing to disclose.

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