Article

Cumulative Patency of Contemporary Fistulas versus Grafts (2000–2010)

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Summary

Background and objectives Comparisons of fistulas and grafts often overlook the high primary failure rate of fistulas. This study compared cumulative patency (time from access creation to permanent failure) of fistulas and grafts.

Design, setting, participants, & measurements Vascular accesses of 1140 hemodialysis patients from two centers (Toronto and London, Ontario, Canada, 2000−2010) were analyzed. Cumulative patency was compared between groups using Kaplan-Meier survival curves and log-rank tests. Hazard ratios (HRs) for fistula failure relative to grafts and 95% confidence intervals (95% CIs) are reported.

Results There were 1012 (88.8%) fistulas and 128 (11.2%) grafts. The primary failure rate was two times greater for fistulas than for grafts: 40% versus 19% ($P<0.001$). Cumulative patency did not differ between fistulas and grafts for the patients' first access (median, 7.4 versus 15.0 months, respectively [HR, 0.99; 95% CI, 0.79−1.23; P=0.85]) or for 600 with a subsequent access (7.0 versus 9.0 months [HR, 0.93; 95% CI, 0.77−1.13; P=0.39]). However, when primary failures were excluded, cumulative patency became significantly longer for fistulas than for grafts for both first and subsequent accesses (61.9 versus 23.8 months [HR, 0.56; 95% CI, 0.43−0.74; $P<0.001$] and 42.8 versus 15.9 months [HR, 0.56; 95% CI, 0.44−0.72; $P<0.001$]). Results were similar for forearm and upper-arm accesses. Compared with functioning fistulas, grafts necessitated twice as many angioplasties (1.4 versus 3.2/1000 days, respectively; $P<0.001$) and significantly more thrombolysis interventions (0.06 versus 0.98/1000 days; $P<0.001$) to maintain patency once matured and successfully used for dialysis.

Conclusions Cumulative patency did not differ between fistulas and grafts; however, grafts necessitated more interventions to maintain functional patency.

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Introduction

Published guidelines on vascular access for hemodialysis recommend the arteriovenous fistula as the preferred vascular access for patients undergoing hemodialysis (1–5). These recommendations were informed by studies showing longer patency and fewer complications for fistulas compared with grafts. However, some limitations of this early evidence have emerged. Once functional, fistulas exhibit greater longevity than grafts, but because new fistulas have a higher primary failure rate than grafts, excluding failed attempts will inflate estimates of cumulative patency for fistulas (6–8). Thirty years ago, the primary failure rate for fistulas was relatively low, around 10% (8–11); however, as fistula creation increased after the National Kidney Foundation-Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI) recommendations (12–16), so have their primary failure rates, which are now as high as 30%−60% (16–20). Primary access failure has numerous attendant consequences: It may delay dialysis initiation, increase catheter dependence, restrict the number of anatomic sites for subsequent accesses, and require additional interventions to salvage the failing access and attempt a new one; all of these put patients at risk of poor health outcomes and increase health care costs (21–23). Such unintended consequences of fistula promotion may arise from attempting fistula creation in higher-risk patients, including the elderly and those with multiple comorbid conditions (17,22). Of note, although the use of grafts declined during the "Fistula First" era, a concomitant increase in central venous catheters has been documented in some studies, particularly in Canada and Australia (16,24–27).

Modern evidence that correctly accounts for failed fistula attempts is needed to accurately compare fistulas and grafts in contemporary dialysis populations. We studied hemodialysis vascular access in patients from two dialysis centers in Toronto and London, Ontario, Canada. We analyzed fistulas and grafts created between 2000 and 2010 and compared their cumulative patencies (time from access creation to permanent failure).

Materials and Methods

Participants and Study Design

We analyzed a cohort of adult hemodialysis patients (three sessions per week) who had a fistula or graft created between January 1, 2000, and June 1, 2010, at the London Health Sciences Centre or the University Health Network, Ontario, Canada. Surgeons in both programs share a common goal of creating fistulas as the initial access when possible (28); however, the clinical or radiologic evaluation of patient suitability for a fistula may vary by surgeon (29). Patient information is entered prospectively into a vascular access database that is managed by a multidisciplinary vascular access team that includes trained data-entry staff. Clinical variables are regularly verified by the vascular access coordinator or director. The database contains information on patient characteristics, type and date of access creation, dates and reasons for access failure, details of access monitoring and surveillance, vascular access–related radiologic interventions and surgeries, and complications.

Measures and Definitions

The primary outcome, cumulative patency, was defined as time from initial access creation to permanent failure (30,31). An access was defined as a primary failure if it was unable to provide prescribed dialysis *via* two-needle cannulation consistently for 1 month within 6 months of its creation, despite interventions to facilitate maturation (31). This included accesses that had early failures for technical reasons, such as perioperative complications or early post-creation thrombosis, or those that simply did not dilate, were too frail to be cannulated, or "failed to mature." For the purpose of survival analysis, accesses that did not have a defining event for access abandonment at an earlier time period (*e.g.*, thrombosis or steal syndrome requiring surgical ligation), but were still unsuitable for dialysis at 6 months were considered to be primary failures and deemed failed at 6 months. A typical dialysis prescription would be a frequency of three times per week for a duration of 3.5–4.5 hours, dialysis blood pump rate of 300–450 ml/min, and dialysate flow rates of 500–800 ml/min. The dialysis blood pump rate, duration, and frequency may vary to achieve a target single pool Kt/V of 1.2.

Comorbid conditions were defined as follows: coronary artery disease; coronary stenosis, documented by angiography or history of myocardial infarction or previous coronary revascularization (angioplasty, stenting, or bypass surgery); peripheral vascular disease, history of lower-extremity revascularization, digit for extremity amputation, or history of claudication and ischemic extremity changes or gangrene; cerebrovascular disease, stroke, or transient ischemic attack documented by computed tomography, magnetic resonance imaging, or diagnosis by a neurologist or two physicians; congestive heart failure documented by echocardiography or chest radiography or symptoms completely resolving with ultrafiltration; and diabetes (if a patient had ever required hypoglycemic agents or insulin or when the diagnosis had been noted in the medical records at least twice by two different physicians). The definition of hyperlipidemia conformed to our Canadian guideline definitions (32,33). Interventions were defined by a radiologic procedure that altered the anatomy of the access in order to maintain its patency (*e.g.*, angioplasty or thrombolysis).

Statistical Analyses

The primary analysis was the cumulative patency of patients' first access; subsequent accesses were evaluated separately. We compared the cumulative patency between fistulas and grafts—with and without primary failures—using Kaplan-Meier survival curves and log-rank tests. Hazard ratios (HRs) for fistula failure relative to grafts and 95% confidence intervals (95% CIs) are reported (HR > 1 reflects a higher failure rate for fistulas relative to grafts). Patients were censored at kidney transplantation, death, withdrawal from therapy, or the end of observation (December 31, 2010). Additional analyses were stratified by access placement (forearm versus upper arm). Finally, we compared the mean number of days that catheters were used for fistulas versus grafts among University Health Network patients. For this exploratory analysis, we analyzed the number of days a catheter was in use from the time a fistula or graft was created and included catheters and their contributing days if they were present and inserted up to 6 months after the access was lost (to account for catheter use that may have been related to loss of an access due to a complication, such as technical surgical failure, failure to mature, or thrombosis). Comparison of Poisson distributions were evaluated using the exact binomial test. Statistical analyses were performed using SAS software, version 9.2 (SAS Institute, Inc., Cary, NC).

Results

From January 2000 through June 2010, 1834 vascular accesses were surgically created. Information on anatomic site was missing for 42 accesses and information on access history was missing for 52. Of 1740 remaining accesses, 1140 were first accesses, including 1012 (88.8%) fistulas and 128 (11.2%) grafts. During this time, 4 patients were lost to follow-up, 206 underwent transplantation, 522 died, and 47 withdrew from treatment. Patient characteristics at the time of first access creation are summarized in Table 1. Patients had an average age of 60 years; 64% were male, 72% were white, 41% had diabetes, and 72% had hypertension. Patients whose first access was a graft were more likely to be female, diabetic, and black; to have a higher body mass index; and to have congestive heart failure. The majority of first accesses were placed in the forearm (59.5% of fistulas and 74.2% of grafts) compared with the upper arm (40.5% of fistulas and 25.8% of grafts) ($P<0.001$).

Primary failure was twice as high for fistulas as for grafts: 402 of 1012 (39.7%) and 24 of 128 (18.8%), respectively ($P<0.001$). For subsequent accesses, primary failure was 2.6 times higher for fistulas than for grafts: 142 of 363 (39.1%) and 36 of 237 (15.2%), respectively ($P<0.001$). When primary failures were included in the analysis, the proportion of first accesses that survived during follow-up did not differ between fistulas and grafts: 350 of 1012 (35%) versus 39 of 128 (31%), respectively; difference in survival, 4 percentage points (95% CI, -5 to 12 percentage points; $P=0.37$). However, when 426 primary failures were excluded from the analysis, fistulas appeared significantly

Table 1. Patient characteristics at time of first access creation in 1140 hemodialysis patients

Characteristic	Overall (*n*=1140)	Dialysis Access		*P* Value[a]
		AV Fistula (*n*=1012)	AV Graft (*n*=128)	
Mean age (yr)	60.0 (18–91)[b]	59.8 (16.4)	61.3 (14.9)	0.34
Age ≥ 65 yr	513 (45.0)	453 (44.8)	60 (46.9)	0.65
Male	734 (64.4)	682 (67.4)	52 (40.6)	<0.001
Race				
White	823 (72.2)	741 (73.2)	82 (64.1)	0.03
Black	70 (6.1)	55 (5.4)	16 (12.5)	0.002
Other	244 (21.5)	214 (21.2)	30 (23.4)	0.90
Mean body mass index (kg/m^2)	27.0 (6.6)	26.5 (6.2)	30.4 (8.0)	<0.0001
Primary renal diagnosis				
Hypertension	230 (20.2)	214 (21.1)	16 (12.5)	0.02
Diabetes	333 (29.2)	280 (27.7)	53 (41.4)	0.001
GN	169 (14.8)	151 (14.9)	18 (14.1)	0.80
Interstitial nephritis	19 (1.7)	16 (1.6)	3 (2.3)	0.53
Hereditary/other	308 (27.0)	277 (27.4)	31 (24.2)	
Unknown	81 (7.1)	74 (7.3)	7 (5.5)	0.44
Median duration of dialysis at time of access creation (mo) (IQR)	0.92 (−3.39 to 5.85)	0.92 (−3.68 to 5.56)	1.51 (−1.05 to 7.40)	0.62
Comorbid conditions				
Diabetes	463 (40.6)	390 (38.5)	73 (57.0)	<0.0001
Hypertension	825 (72.4)	727 (71.8)	98 (76.6)	0.26
Coronary artery disease	274 (24.0)	237 (23.4)	37 (28.9)	0.17
Congestive heart failure	148 (13.0)	123 (12.1)	25 (19.5)	0.02
Peripheral vascular disease	90 (7.9)	79 (7.8)	11 (8.6)	0.76
Cerebrovascular disease	107 (9.4)	92 (9.0)	15 (11.7)	0.33

Unless otherwise noted, values are numbers (percentages). Means are given with SDs. AV, arteriovenous; IQR, interquartile range.
[a]Variables were compared using the chi-squared test or *t* test as appropriate.
[b]Range.

more likely to survive than grafts: 350 of 610 (57%) versus 39 of 104 (37%); difference in survival, 20 percentage points (95% CI, 9–29 percentage points; *P*<0.001).

Overall, the median cumulative patency after initial access creation was 8.3 months. As shown in Figure 1A, cumulative patency did not differ between fistulas and grafts: median, 7.4 versus 15.0 months, respectively (HR, 0.99; 95% CI, 0.79−1.23; *P*=0.85); however, when primary failures were excluded (Figure 1B), cumulative patency became significantly longer for fistulas than for grafts: median, 61.9 versus 23.8 months (HR, 0.56; 95% CI, 0.43−0.74; *P*<0.001). A similar pattern was seen in 600 patients who had a subsequent access created: Cumulative patency did not differ between fistulas and grafts (median, 7.0 versus 9.0 months [HR, 0.93; 95% CI, 0.77−1.13; *P*=0.39]) unless primary failures were excluded (median, 42.8 versus 15.9 months [HR, 0.56; 95% CI, 0.44−0.72]; *P*<0.001).

In addition, for 697 patients whose first access was a forearm access (Figure 2, A and B), cumulative patency did not differ between fistulas and grafts (median, 6.0 versus 14.2 months [HR, 0.96; 95% CI, 0.74−1.24; *P*=0.64]) unless primary failures ere excluded (median, 76.6 versus 23.7 months [HR, 0.47; 95% CI, 0.34−0.66; *P*<0.001]). When restricted to 443 upper-arm accesses (Figure 3, A and B), cumulative patency did not differ between fistulas and grafts (median, 9.9 versus 20.1 months [HR, 1.22; 95% CI, 0.77−1.90; *P*=0.37]), regardless of whether primary failures were excluded (median, 46.9 versus 38.2 months [HR, 0.94; 95% CI, 0.53−1.67; *P*=0.83]).

Interventions

The average number of catheter days was slightly higher for fistulas than grafts for the first access created (250 days versus 239 days), although the difference was not statistically significant (*P*=0.80). However, this difference widened and approached significance when subsequent accesses were considered: 279 days for fistulas versus 204 days for grafts (*P*=0.05). Overall, compared with fistulas, grafts necessitated significantly more interventions to maintain patency after cannulation: twice as many angioplasties (1.4 versus 3.2/1000 days, respectively; *P*<0.001) and significantly more thrombolysis interventions (0.06 versus 0.98/1000 days, respectively; *P*<0.001).

Discussion

In this analysis of hemodialysis patients who had a fistula or graft created after 2000, primary failure of vascular access was two times greater for fistulas than for grafts (40% versus 19%), and cumulative patency for fistulas was not superior to that for grafts—unless primary

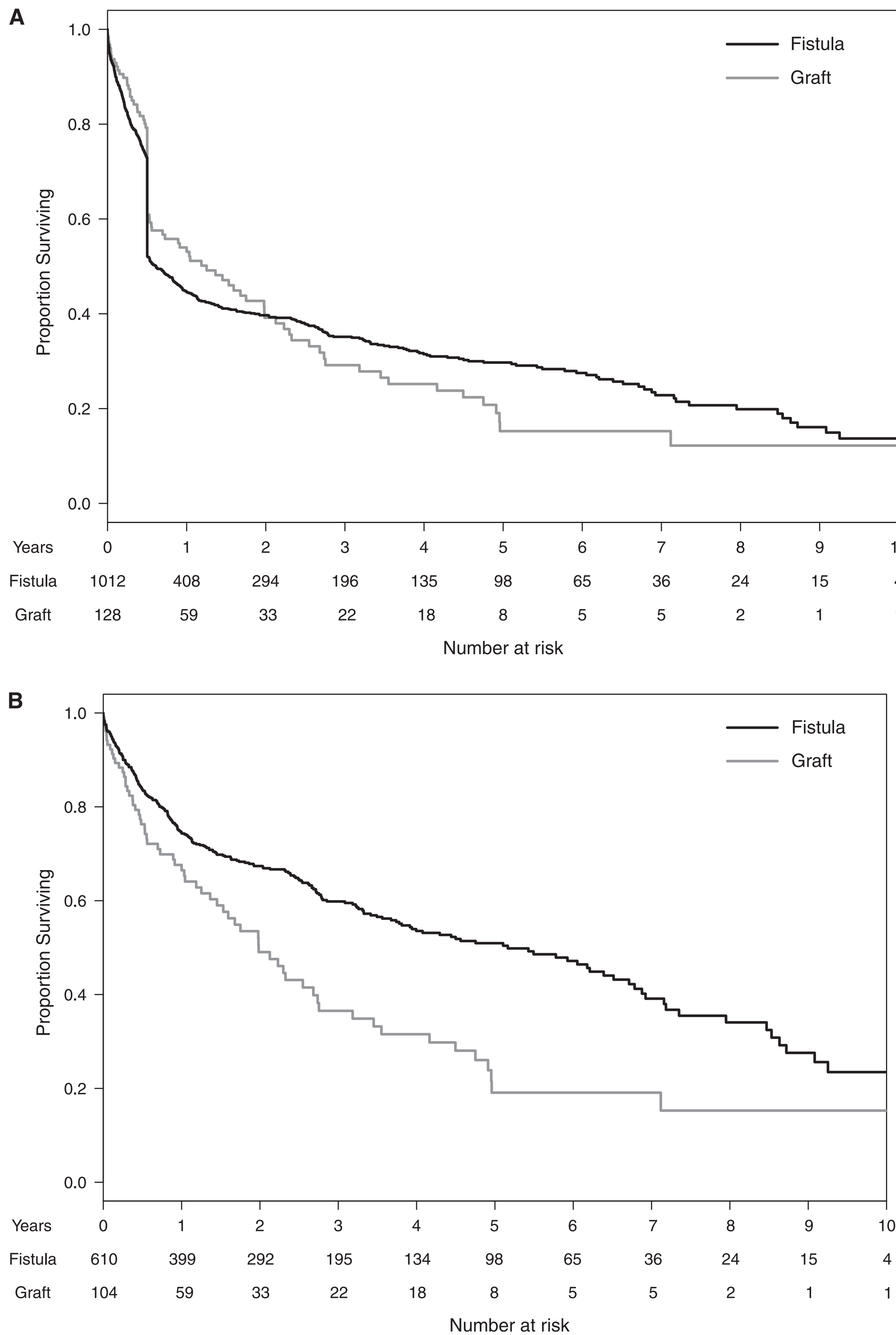

Figure 1. | Survival curves of cumulative patency in hemodialysis patients. (A) 1140 patients: arteriovenous fistulas versus arteriovenous grafts (hazard ratio [HR], 0.99; 95% confidence interval [CI], 0.79–1.23). (B) 714 patients after excluding 426 primary failures: arteriovenous fistulas versus arteriovenous grafts (HR, 0.56; 95% CI, 0.43–0.74).

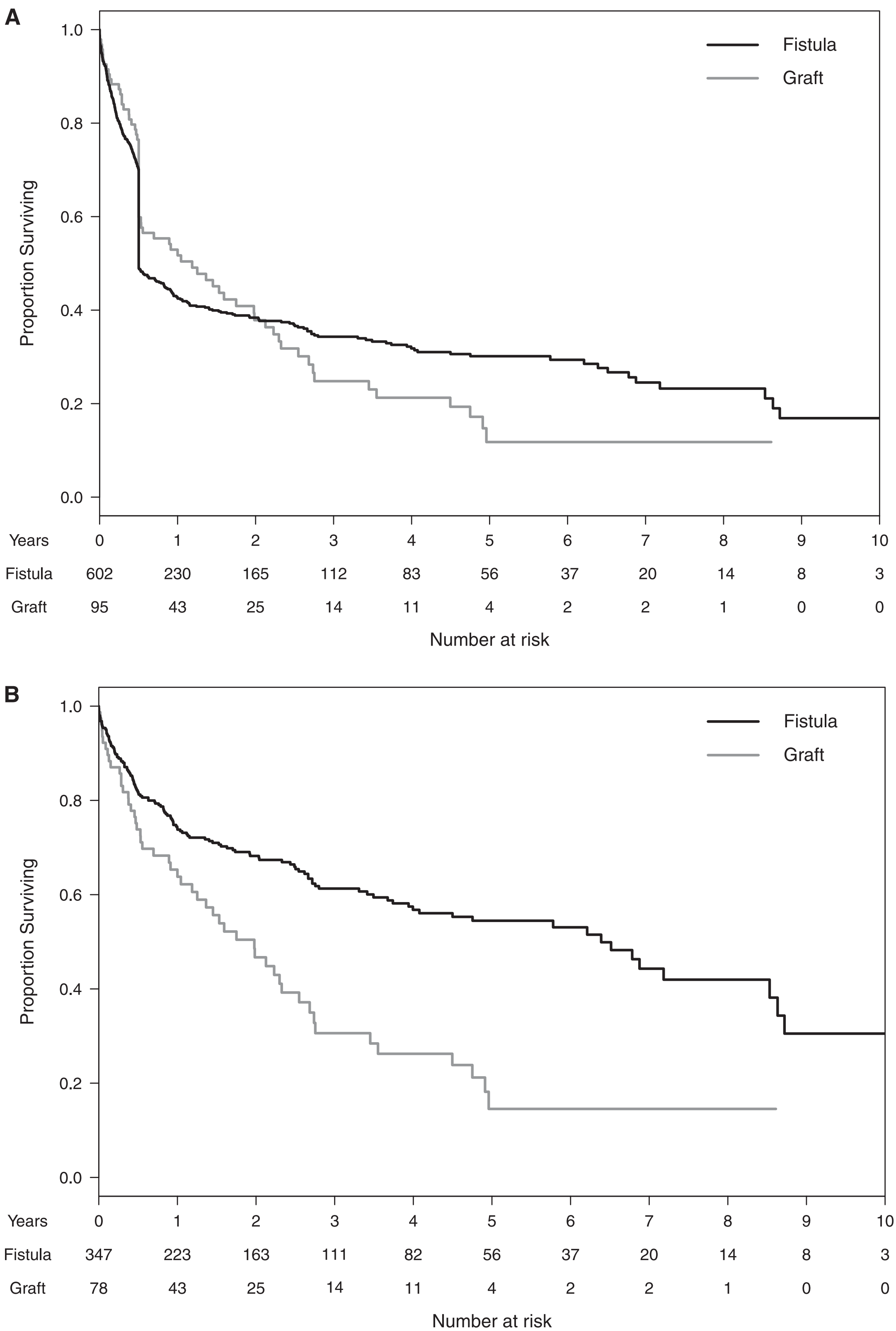

Figure 2. | Survival curves of cumulative patency in hemodialysis patients with forearm access. (A) 697 patients: arteriovenous fistulas versus arteriovenous grafts (hazard ratio [HR], 0.96; 95% confidence interval [CI], 0.74−1.24; $P=0.64$). (B) 425 patients after excluding 272 primary failures: arteriovenous fistulas versus arteriovenous grafts (HR, 0.47; 95% CI, 0.34−0.66; $P<0.001$).

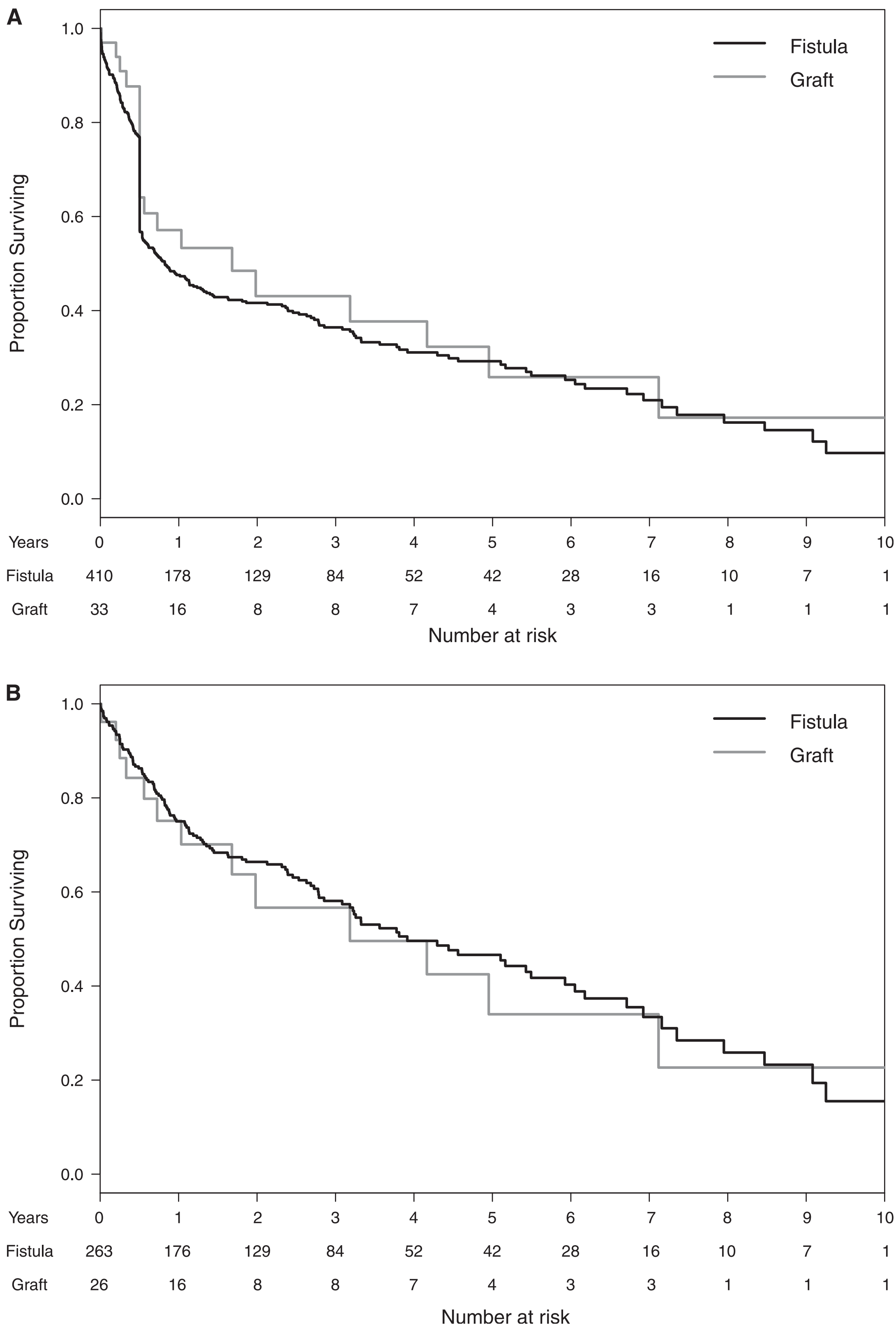

Figure 3. | **Survival curves of cumulative patency in hemodialysis patients with upper-arm access.** (A) 443 patients: arteriovenous fistulas versus arteriovenous grafts (hazard ratio [HR], 1.22; 95% confidence interval [CI], 0.77−1.90; $P=0.37$). (B) 289 patients after excluding 154 primary failures: arteriovenous fistulas versus arteriovenous grafts (HR, 0.94; 95% CI, 0.53−1.67; P=0.83).

failures were excluded. This pattern was consistent for forearm accesses and those with subsequent access attempts. Although the cumulative patency did not differ between fistulas and grafts, grafts necessitated significantly more interventions to maintain patency after successful cannulation.

The primary failure rate for fistulas in this study (40%) is similar to that in other studies published since 2003, which report primary failure rates ranging from 30% to 60% (6,16–20,34). As shown in this study and others, the cumulative patency of functional fistulas is considerably better than that of grafts (median duration of patency, approximately 3−5 years versus 1−2 years). As well, the need for interventions to maintain patency is markedly reduced among fistulas relative to grafts (18,22,34,35). Thus, maximizing the number of patients who initiate dialysis with a mature fistula suitable for cannulation is an important goal. The "Fistula First" initiative, which launched in 2003, has been successful at increasing fistula use in the United States: Between 2000 and 2010, fistula use more than doubled, increasing from 24% to 56%, whereas graft use decreased from 58% to 22% (16,22,36,37). The success of the initiative was tempered by an initial increase in catheter use, but more recent analyses report declining rates since 2007 (16,22,27,37). However, increasing rates of catheter use are documented in Canadian and Australian patients—and in both Canada and the United States approximately 80% of patients still initiate hemodialysis with a catheter (24–26). In addition, for patients with failed fistulas, Canadian nephrologists are more likely to consider a catheter rather than a graft, but the reverse is true for nephrologists in the United States (38). This is concerning because catheter use is associated with an increased risk for infection-related hospitalizations, frequent catheter malfunction due to thrombosis, inflammation, and mortality (27,39–42). To be most effective, a national vascular access initiative should pursue the combined goal of maximizing use of functional fistulas while minimizing catheter use (27,39). Whereas a functioning fistula is superior to a graft, a nonfunctioning fistula with prolonged catheter dependence is not. In our study, the average number of catheter days was slightly higher for fistulas than for grafts, although this finding was not statistically significant. These data suggest that fistula use did not reduce exposure to catheters, and future research should look at this issue more carefully. For example, in addition to comparing cumulative patency and complication-free days, researchers should also evaluate catheter-free days.

Complications from vascular access dysfunction represent the leading cause of morbidity among hemodialysis patients, accounting for 16%−18% of dialysis-related hospital admissions in Canada and the United States (42–44). Attempting fistula placement in a wider spectrum of patients (some of whom may be only marginal candidates) may have led to the increased rate of primary failure for fistulas and greater exposure to catheters (16,22). Fistula failure not only denies patients a functional access but also reduces the number of possible sites for an alternate access and exposes the patients to risks from interventions directed at salvaging the failing access (20). Further, these failures may lead patients to doubt the overall benefit of fistulas. Patient refusal is a significant barrier to fistula creation: Currently, up to 30% of eligible patients decline fistula creation (24,45–47). In a novel qualitative study conducted by Xi *et al.*, negative personal or vicarious experience with a fistula emerged as a major reason for patient refusal of a fistula (45).

Current guidelines published by the NKF-K/DOQI and the Canadian Society of Nephrology list the order of vascular access preference as forearm (radiocephalic) fistula, followed by brachiocephalic fistula, transposed brachiobasilic fistula, and, finally, a graft (5,48). Although many believe that the evidence for fistula superiority is unequivocal—and that conducting a randomized, controlled trial would be unethical—our study and others provide evidence of equipoise (20,22,34,49–51). Collectively, these studies show that there are nontrivial tradeoffs between fistulas and grafts; these tradeoffs favor fistula creation in some patients and grafts in others. Some studies show that vessel size is an important predictor of fistula patency (20,52), but in others, routine preoperative vessel mapping failed to improve rates of fistula maturation (6,17,19). Thus, evidence to date leads us to emphasize the importance of considering four key factors when choosing an access: (*1*) the likelihood of early access complications and primary failure; (*2*) the likelihood of later access complications, such as stenosis and thrombosis; (*3*) catheter-related complications, such as bacteremia and central vein stenosis; and (*4*) expected patient survival (22). The risk of fistula failure is greatest among older patients, obese and/or female patients, those with substantial vascular comorbidity, and those with a prior failed fistula (7,19,35).

In our study, grafts were more likely to be placed in such high-risk patients, yet these patients achieved cumulative survival similar to that in lower-risk patients who received fistulas. Selective use of grafts in high-risk patients may afford similar cumulative patency with reduced exposure to the risks associated with catheters (22). A nonselective "Fistula First" approach among certain populations, such as elderly patients, may be particularly ill advised given low fistula functionality and high patient mortality in this group (53,54). For example, in a study of elderly dialysis patients (53), 58% of patients older than 80 years died within 18 months of initiating dialysis; of those who died, 89% started with a catheter and 70% had a fistula created. However, these patients all died before their fistulas could be cannulated. From the patient's perspective, this may not be seen as "improving vascular access outcomes" (1). These results are concerning given that elderly patients represent the fastest-growing segment of the ESRD population.

This study has some limitations. The results reflect a retrospective analysis of clinical care dialysis data; however, data on outcome assessment from each center were entered prospectively into the database by trained personnel. We analyzed data from only two centers, which may limit the generalizability of our results. Other studies have documented considerable intercenter variability in vascular access use and outcomes; this variability is attributed to variation in surgical skill and practices, the cohesiveness of the vascular access team, dialysis management resources and policies (including the availability and quality of predialysis care), presence of a vascular access case manager, prevalence of late referrals, time to cannulation, and patient comorbidity (8,27,37,55,56). Although a multicenter analysis of a national database may provide greater external validity, our results confirm trends reported in other studies. As well, our results are not confounded by disparities in access to health insurance. Our data did not address the need for intervention to achieve functionality before access use. This may have resulted in fewer interventions documented for fistulas, which typically necessitate more interventions for maturation than do grafts (16,49). Finally, access choice was not standardized, and the clinical or radiologic evaluation of patient suitability for a fistula may have varied by surgeon.

In this study and others, the precise failure time of accesses deemed to be primary failures is often unclear—these accesses are in place and may be used once or twice during a 6-month period but never mature sufficiently to provide reliable dialysis. For the purpose of survival analysis, primary failures were allowed a survival time of 6 months if failure was not clearly evident before this time (*e.g.*, accesses that did not thrombose at an earlier time period but were still unsuitable for dialysis at 6 months were considered to be primary failures and deemed to have failed at 6 months). The overall survival time of an access includes the time to maturation in addition to time of use, thereby allowing the maturation time to contribute to the overall survival time for successful accesses; however, excluding it for primary failures would selectively inflate the cumulative patency of successful accesses. Further, because fistulas have a higher primary failure rate than grafts, excluding the maturation time for primary failures could differentially inflate the cumulative patency for grafts relative to fistulas. However, even though our analysis granted a minimum maturation time for primary failures, cumulative patency of fistulas and grafts was similar.

In conclusion, fistulas in this study did not demonstrate better cumulative patency than grafts unless primary failures were excluded; however, grafts required more interventions to maintain patency once cannulated. Optimizing vascular access management is an extraordinarily complex task that does not appear amenable to a singular strategy such as "Fistula First" (57). Perhaps broadening this strategy to concurrently emphasize "catheters last" would allow greater consideration for grafts among patients at high risk for fistula failure. Taken together, the results of this study and others provide the equipoise needed to support a randomized, controlled trial comparing fistulas and grafts in the subpopulation of dialysis patients for whom the superiority of fistulas over grafts is uncertain (22).

Disclosures

None.

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