International Differences in the Location and Use of Arteriovenous Accesses Created for Hemodialysis: Results From the Dialysis Outcomes and Practice Patterns Study (DOPPS)

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Background: Vascular access practice is strongly associated with clinical outcomes. There is substantial international variation in the use of arteriovenous fistulas (AVFs) and grafts (AVGs), as well as AVF maturation time and location.

Study Design: Prospective cohort study.

Setting & Participants: Hemodialysis patients participating in the prospective Dialysis Outcomes and Practice Patterns Study (DOPPS) from the United States, Japan, and Europe/ANZ (Belgium, France, Germany, Italy, Spain, Sweden, United Kingdom, Australia, and New Zealand), including 3,850 patients receiving 4,247 new AVFs and 842 patients receiving 1,129 new AVGs in 2009 to 2015. AVF location trends were based on 38,868 AVFs recorded in DOPPS 1 to 5 cross-sections (1996-2015).

Predictors: Demographics, comorbid conditions, dialysis vintage, body mass index, facility percentage AVF use, median blood flow rate, and AVF location.

Outcomes: AVF location; successful AVF/AVG use (≥30 days of continuous use); time-to-first successful AVF/AVG use (maturation).

Results: During DOPPS 1 to 5, the percentage of AVFs created in the lower arm was consistently ≥93% in Japan and 65% to 77% in Europe/ANZ, but in the United States, this value declined from 70% (DOPPS 1) to 32% (DOPPS 5). Patient characteristics associated with AVF location differed by region. Successful AVF use was 87% in Japan, 67% in Europe/ANZ, and 64% in the United States, whereas successful AVG use was 86%, 75%, and 78%, respectively. Successful AVF use was greater for upper- versus lower-arm AVFs in the United States, with little difference in Europe/ANZ and the opposite pattern in Japan. Median time until first successful AVF use was 10 days in Japan, 46 days in Europe/ANZ, and 82 days in United States; until first successful AVG use: 6, 24, and 29 days, respectively.

Limitations: Potential measurement error related to chart data abstraction in multiple hemodialysis facilities.

Conclusions: Large international differences exist in AVF location, predictors of AVF location, successful use of AVFs, and time to first AVF/AVG use, challenging what constitutes best practice. The large US shift from lower- to upper-arm AVFs raises serious concerns about long-term health implications for some patients and how policies and practices aimed at increasing AVF use have affected AVF placement location.

Complete author and article information provided before references.

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The ability to deliver maintenance hemodialysis (HD) therapy is dependent on a functional vascular access. There is broad consensus across many national organizations that a well-functioning arteriovenous (AV) fistula (AVF) is the preferred access for HD patients, but vascular access should be individualized for a patient's health status and other considerations.[1-4]

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The Dialysis Outcomes and Practice Patterns Study (DOPPS) is an international prospective cohort study of HD practices and patient outcomes that has been ongoing since 1996. Study patients 18 years or older and HD facilities are randomly selected to be representative of HD patients and practices in each nation. In recent work from DOPPS phase 5 (2012-2014), large variations were seen across 21 countries in use of an AVF (range, 49%-92%), AV graft (AVG) (range, 2%-18%), and central venous catheter (range, 2%-49%).[5]

Survival of AVFs following successful first use (cumulative functional survival) has also been shown to differ across the 3 continental regions in DOPPS, with Japan displaying longer AVF survival compared with Europe, Australia, New Zealand (Europe/ANZ), and North America.[6] AVF survival may be affected by both dialysis and practitioner practices. For example, Asano et al[6] found lower facility median blood flow rates to be associated with longer cumulative functional AVF survival, with median blood flow rates differing greatly by region (200 mL/min in Japan, 300 mL/min in Europe/ANZ, and 400 mL/min in North America). Furthermore, Saran et al[7] described large international differences in exposure of surgical trainees to AVF creation during training (DOPPS phase 2 [2002-2004]), with greater surgical training in AVF creation associated with a nearly 1.5-fold lower hazard ratio (HR) of primary AVF failure.

Given the large international variation in vascular access use and outcomes, we sought to further understand international differences in the following: (1) AVF creation

location (upper vs lower arm), (2) trends in AVF location from DOPPS phases 1 to 5 (1996-2015), and (3) successful use of newly created AVFs and AVGs (together referred to as "AV accesses").

Methods

Overview

Since 1996, five DOPPS phases have been completed, with the study design published[8,9] and each phase approved by national and/or local ethics committees as required by local ethics regulations. Informed patient consent has been obtained as required by pertinent ethics committees.

Primary analyses were based on study samples shown in Figure 1. Analyses excluded the 3.7% of AV accesses placed in nonarm locations or that lacked placement location information in DOPPS phases 4 to 5. Data are not shown for AVG creation location due to possible ambiguity in reporting arm placement location for some AVGs. Patient demographics and comorbid conditions were reported at DOPPS entry. Vascular access type (in use or placed), vascular access location, dates of creation, first use, vascular access failures or removal, and vascular access–related procedures were collected throughout follow-up. In DOPPS phase 5, complete vascular access information was not available in the United States for one large dialysis organization, limiting its inclusion for only some analyses, as noted in figures and tables. Despite this, patterns of AVF placement and successful use were similar in the United States in DOPPS phase 4 versus phase 5.

Successful AV Access Use

Successful AV access use was defined as a newly created AV access being used for 30 or more continuous days (for typically thrice-weekly HD) during follow-up in DOPPS phases 4 to 5. Successful AVF use was calculated using 2 approaches: (1) primary calculation: among all newly created AVFs (N = 2,744) having 30 or more days of follow-up after AVF creation, the percentage successfully used for HD; this approach serves to inform from a resource perspective what percentage of newly created AV accesses are actually used; and (2) secondary calculation: among all newly created AVFs having 30 or more days of follow-up after AVF creation, the percentage successfully used for HD when meeting this additional requirement: within 7 months of AVF creation, an AVF either displayed successful use, failed to display successful use, or displayed nonfunctionality (reported as failed or replaced [without use] by another AV access). The 7-month period for successful AVF use was based on the 90th percentile of AVF maturation times observed in the United States in DOPPS phases 4 to 5 (Fig 2A) because maturation times were

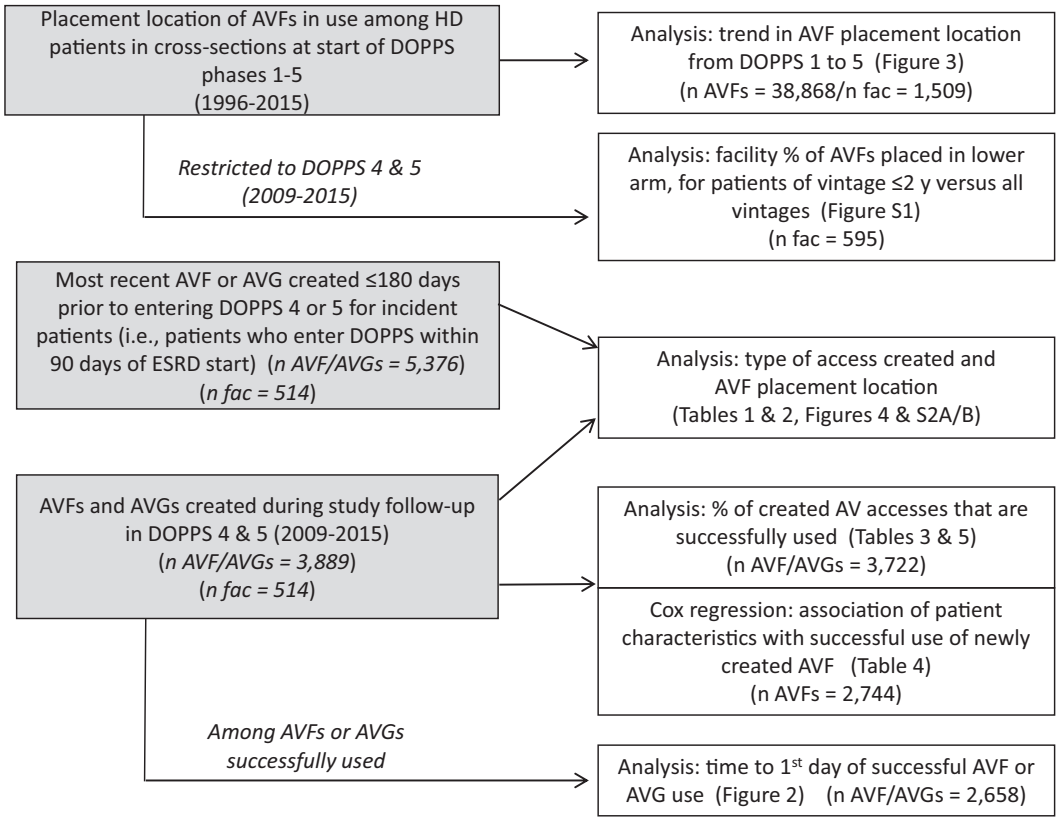


Figure 1. Description of samples used for various analyses. Abbreviations: AV, arteriovenous; AVF, arteriovenous fistula; AVG, arteriovenous graft; DOPPS, Dialysis Outcomes and Practice Patterns Study; ESRD, end-stage renal disease.

longer in the United States than elsewhere. This secondary approach estimates the percentage of newly created AVFs successfully used if given sufficient time to mature.

Successful AVG use was also calculated using these 2 approaches. However, for the secondary approach, 3 rather than 7 months were required to demonstrate successful AVG use based on the 90th percentile of AVG maturation times observed for the United States.

Statistical Analyses

Generalized estimating equations with a logit link and assuming a compound symmetry covariance structure (logistic regression) were used to evaluate outcomes noted in Results. Cox regression was applied to investigate predictors of time to successful AVF use by DOPPS region. Follow-up time started on the AVF creation date; date of successful use was day 30 of continuous AVF use after creation. Follow-up time was censored at the earliest date of the following: last follow-up, last vascular access data reported, use of a subsequent AV access, or study departure for any reason (death, transplantation, modality change, kidney function recovery, withdrawal, or transfer to another facility). An HR > 1 indicates greater successful AV access use or shorter time to successful use. Model predictor variables were chosen a priori based on findings from prior published studies. Extensive model-building analyses have been performed to determine whether inclusion of particular covariates in the models affected the association of the outcome with other included covariates. Cardiovascular disease was defined as a history of coronary artery, cerebrovascular, or other cardiovascular disease. Facility percentage AVF use and facility median blood flow rates were based on a baseline cross-section of study patients within each facility in DOPPS phases 4 to 5. Cox and logistic regression models accounted for multiple AV accesses per patient and for clustering of patients within facilities. Cox models used the sandwich estimator[10] to account for clustering. All analyses were performed using SAS, version 9.4 (SAS Institute).

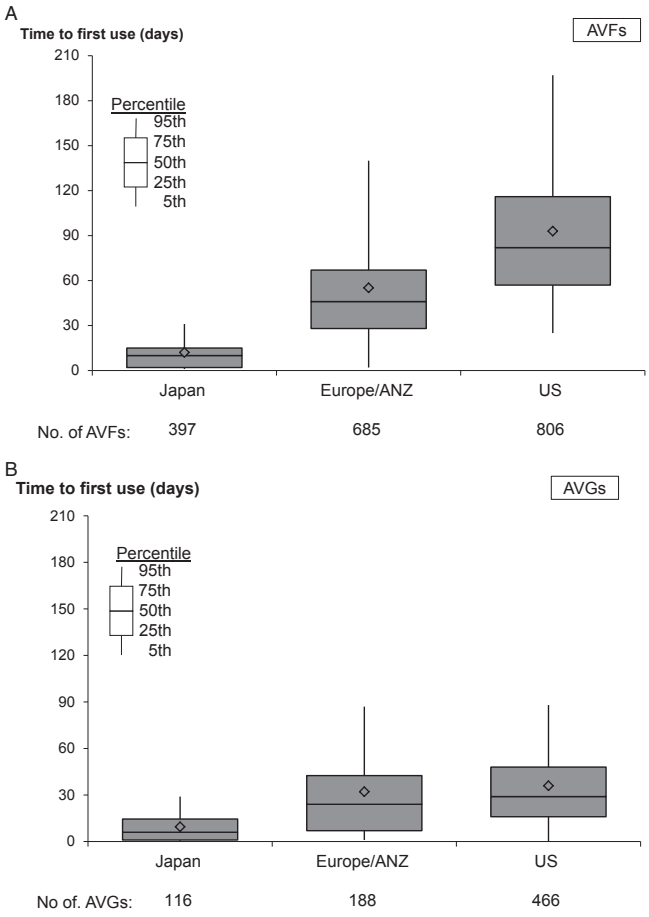


Figure 2. Distribution of time to first day of successful arteriovenous (AV) access use by region among AV accesses that were successfully used for 30 or more days: (A) AV fistulas (AVFs) and (B) AV grafts (AVGs). Sample: restricted to AVFs/AVGs that were created within the study and were successfully used for at least 30 days; open diamond represents the mean. Europe/Australia and New Zealand (ANZ) includes Belgium, France, Germany, Italy, Spain, Sweden, and United Kingdom.

Results

International Trends in AVF Creation Location (DOPPS 1-5) and Facility Variation

In DOPPS phases 1 to 5, nearly all AVFs were located in an upper-extremity location (>96%). Cross-sectional data (Fig 3) indicated large international differences in the location of arm AVFs: in Japan, ≥93% were located in the lower arm throughout DOPPS phases 1 to 5; in Europe/ANZ, 77% of AVFs were in the lower arm in DOPPS phases 1 to 2, declining to approximately 65% in DOPPS phases 4 to 5; in contrast, US practice switched from predominantly lower-arm AVFs in DOPPS phase 1 (70%) to a minority of lower-arm AVFs by DOPPS phase 5 (32%). Similar international trends were seen when restricted to patients of dialysis vintage less than 90 days.

In DOPPS phases 4 to 5 (2009-2015), facility variation in percentage of lower-arm AVFs (Fig S1) indicated: (Fig S1A) a tight distribution within Japan, with 95% (interquartile range [IQR], 91%-100%) of AVFs in the lower arm in the median facility; (Fig S1B) broad variation across facilities in the 11 Europe/ANZ countries, with 67% (IQR, 53%-78%) of arm AVFs located in the lower arm in the median facility; and (Fig S1C) large (~5-fold) variation across US facilities, with 38% (IQR, 23%-47%) of arm AVFs located in the lower arm in the median facility.

Predictors of AVF Location by International Region: DOPPS 4 and 5

Additional aspects of AV access placement location were investigated in DOPPS phases 4 and 5 (Table 1), with most patients (86%) contributing only one AV access to these analyses. Among AVFs, lower-arm location was highest in Japan (89%) versus 60% in Europe/ANZ and 34% in the United States, despite the United States having the

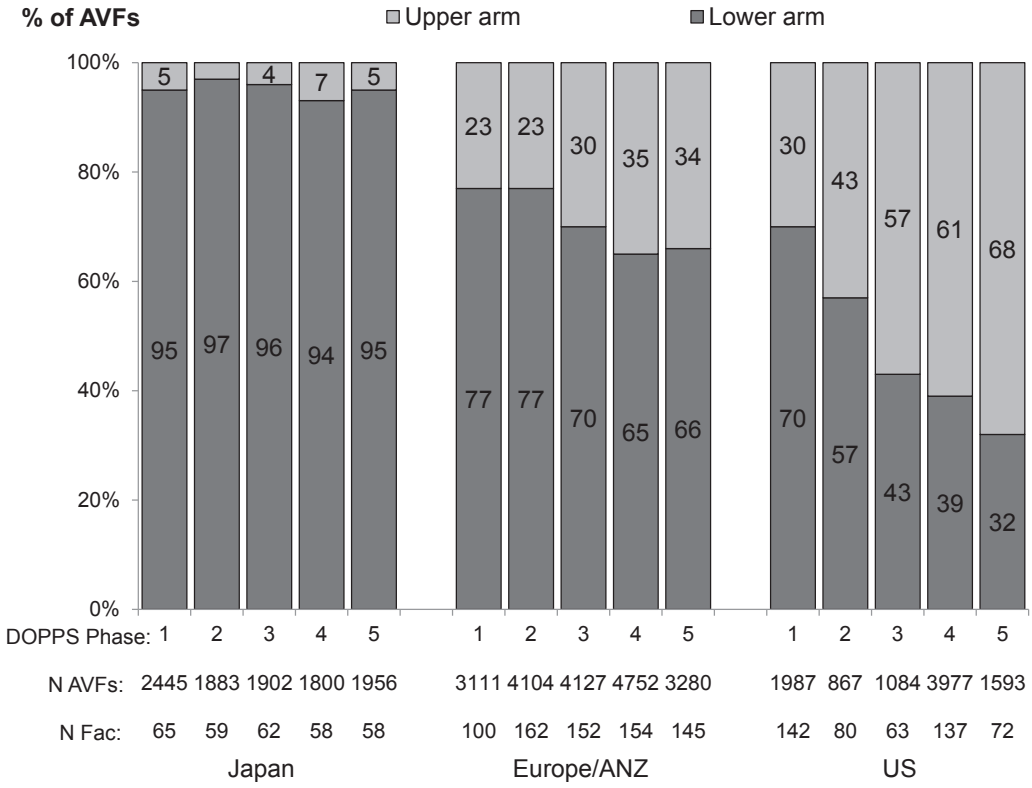


Figure 3. Trend in arteriovenous fistula (AVF) location in the upper versus lower arm from the Dialysis Outcomes and Practice Patterns Study (DOPPS) 1 (1996-2001) to DOPPS 5 (2012-2015), by region. Based on location of AVF in use at study entry in the initial round of data collection for each study phase: DOPPS 1 (1996-2001), DOPPS 2 (2002-2004), DOPPS 3 (2005-2008), DOPPS 4 (2009-2012), DOPPS 5 (2012-2015). Europe/Australia and New Zealand (ANZ) includes France, Germany, Italy, Spain, and United Kingdom (DOPPS 1) and ANZ, Belgium, France, Germany, Italy, Spain, Sweden, and United Kingdom (DOPPS 2-5). Results were similar when Europe/ANZ was restricted to countries present in all phases. Abbreviation: Fac, facilities.

youngest mean age by several years. Diabetes prevalence was highest for US patients, differing little among US patients having lower- versus upper-arm AVFs.

AVGs constituted 12% to 13% of all created AV accesses in DOPPS phases 4 to 5 in Europe/ANZ and Japan versus 25% in the United States. Among patients having a newly created AVG versus AVF: (1) median dialysis vintage was longer and percentage of males was lower in all 3 regions, and (2) mean age was slightly older in the United States and Europe/ANZ, with the opposite seen in Japan.

In subgroup analyses (Fig 4A and B), AVFs were located in the lower arm more often for males than females in each age group in the United States and Europe/ANZ, with little difference seen by sex in Japan. Among male and female HD patients, the percentage of AVFs located in the lower arm tended to be highest for patients younger than 55 years in all 3 study regions, with little difference for those aged 55 to 74 versus older than 74 years in the United States and Europe/ANZ. Similar results were seen when restricted to AVFs created within 2 years of initiating HD therapy (Fig S2).

Logistic regression analyses (Table 2) indicated that a lower-arm AVF location was less likely with longer dialysis vintage in all regions and for females in the United States and Europe/ANZ, but not in Japan. Furthermore, lower-arm AVFs were less likely in: (1) people with diabetes in Europe/ANZ and (2) patients with peripheral vascular disease in the United States, possibly also in Europe/ANZ. Older age was weakly associated with possible lower odds of lower-arm AVF placement. Similar findings were observed when restricted to AVFs created within the first 2 years of initiating HD therapy (results not shown).

Successful Use of Newly Created AVFs by International Region: DOPPS 4 and 5

Successful AV access use was defined as using a newly created AV access for 30 or more continuous days in DOPPS phases 4 to 5. Successful AVF use varied from 87% in Japan, 67% in Europe/ANZ, and 64% in the United States in analyses without follow-up time requirements beyond 30 days (Table 3, upper half).

By secondary calculation, which allowed AVFs to have up to 7 months to demonstrate successful AVF use after creation (Table 3, lower half), 89% of AVFs in Japan, 76% in Europe/ANZ, and 77% in the United States were

Table 1. Characteristics of Study Patients at Enrollment Having a Newly Created AVF Versus AVG, by DOPPS Region and AVF Location

Characteristic	Japan			Europe/ANZ[a]			United States		
	Upper-Arm AVF	Lower-Arm AVF	AVG	Upper-Arm AVF	Lower-Arm AVF	AVG	Upper-Arm AVF	Lower-Arm AVF	AVG
No. of patients	70	651	107	587	988	211	1,015	539	524
Proportion of patients in DOPPS region	8%	79%	13%	33%	55%	12%	49%	26%	25%
No. of AV accesses[b]	85	722	155	691	1,040	284	1,134	575	690
Age, y	68 ± 13	65 ± 13	66 ± 13	65 ± 14	64 ± 15	66 ± 14	62 ± 15	61 ± 15	64 ± 15
Age category									
<55 y	14%	18%	18%	22%	25%	22%	29%	32%	26%
55-74 y	46%	58%	52%	48%	44%	45%	49%	46%	49%
≥75 y	39%	24%	30%	29%	30%	33%	22%	22%	25%
Dialysis vintage, y	0.6 [0.2-7.1]	0.2 [0.1-1.8]	3.5 [0.4-12.4]	0.2 [0.1-1.5]	0.2 [0.1-0.4]	1.8 [0.3-5.8]	0.2 [0.1-0.8]	0.2 [0.1-0.3]	0.4 [0.2-2.4]
Male sex	63%	67%	55%	61%	73%	50%	54%	66%	45%
Black race	—	—	—	4%	2%	6%	26%	22%	33%
BMI, kg/m^2	21.4 ± 3.2	21.8 ± 3.7	21.4 ± 3.7	26.6 ± 5.6	26.7 ± 5.7	27.1 ± 5.9	29.1 ± 7.3	28.9 ± 7.0	28.4 ± 7.6
Comorbid conditions									
Coronary artery disease	34%	26%	32%	37%	34%	34%	32%	30%	33%
Other cardiovascular disease	33%	23%	26%	31%	29%	32%	20%	16%	19%
Congestive heart failure	35%	21%	25%	25%	19%	26%	36%	29%	34%
Cerebrovascular disease	9%	11%	13%	15%	13%	16%	11%	7%	10%
Diabetes	45%	50%	42%	45%	36%	44%	64%	63%	68%
Hypertension	86%	84%	85%	88%	88%	82%	82%	80%	82%
Peripheral vascular disease	19%	13%	13%	32%	24%	35%	22%	16%	20%

Note: Values for continuous variables given as mean ± standard deviation or median [interquartile range]. Restricted to the initial AV access created in DOPPS 4 (2009-2011) and DOPPS 5 (2012-2015). In the case of incident patients (defined as new to ESRD within 90 days of study enrollment), AVFs and AVGs created within 180 days before study entry were included in the analyses.

Abbreviations: ANZ, Australia and New Zealand; AV, arteriovenous; AVF, arteriovenous fistula; AVG, arteriovenous graft; BMI, body mass index; DOPPS, Dialysis Outcomes and Practice Patterns Study; ESRD, end-stage renal disease.

[a]Results by each country rather than only for Europe/ANZ, Japan, and the United States are provided in Table S1.

[b]Most patients (86%) had only 1 AVF or AVG created.

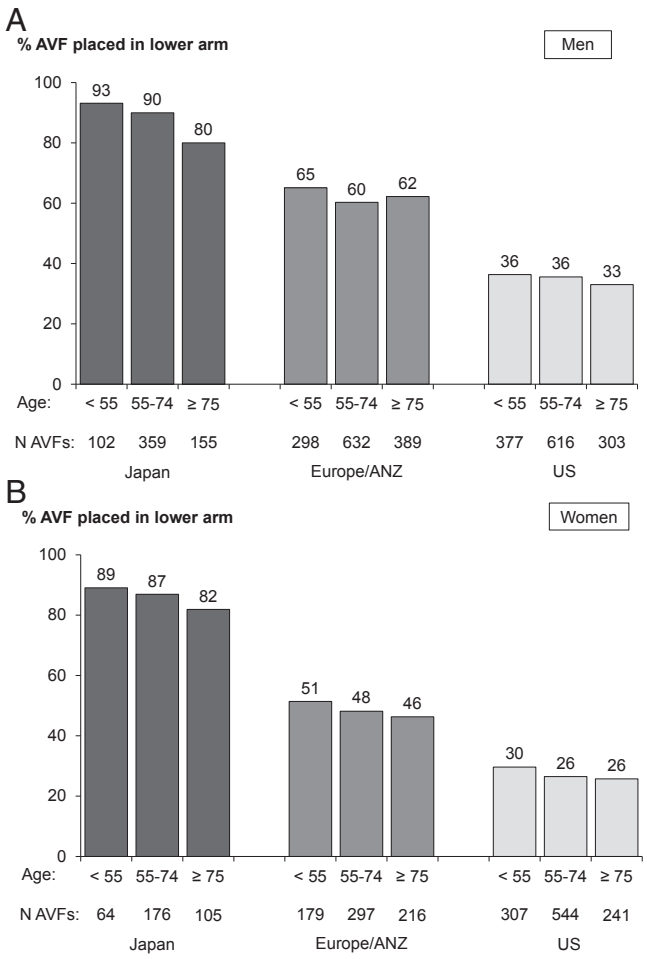


Figure 4. Percentage of new arteriovenous fistulas (AVFs) located in the lower arm in male versus female hemodialysis patients by age group, for all new AVFs created for the study cohort. (A) Males and (B) females. AVFs created within 180 days before study entry were included for incident patients (ie, patients who entered the Dialysis Outcomes and Practice Patterns Study [DOPPS] within 90 days of end-stage renal disease start).

successfully used. Among AVFs having any use (≥1 day), at least 97% were used for 30 or more days in all regions, indicating that very few AVFs failed within 30 days of first use. In both analytic approaches, AVF use was more successful for upper- versus lower-arm AVFs in the United States and Europe/ANZ, with the opposite seen in Japan.

Multivariate Cox regression of time to successful AVF use (Table 4) indicated differing associations of covariates with the outcome by region. Greater successful AVF use was seen: (1) for males versus females in Europe/ANZ and the United States, but not in Japan; (2) for upper- versus lower-arm AVFs in the United States, with the opposite seen in Japan and no difference seen in Europe/ANZ; and (3) in Europe/ANZ patients without cardiovascular disease and in Europe/ANZ facilities having a higher percentage of AVF use. Model-building analyses indicated that the order of adding covariates into the models had little impact on the strength and direction of the associations of key predictors with the outcome of successful AVF use (Table S2). Covariate associations with successful AVF use were also examined in logistic regression analyses and found to be consistent with the direction of association seen in these Cox models for key findings (Table S3).

Successful Use of Newly Created AVGs by International Region: DOPPS 4 and 5

Successful use of AVGs created in DOPPS phases 4 and 5 was determined in each international region (Table 5). Analyses without follow-up time requirements (Table 5, upper half) indicated that successful AVG use varied from 86% in Japan, 75% in Europe/ANZ, and 78% in the United States.

The alternative calculation allowed AVGs up to 3 months after creation to demonstrate successful AVG use (Table 5, lower half) and indicated successful AVG use of 89% in Japan, 78% in Europe/ANZ, and 83% in the United States. Notably, 3% to 6% of newly created AVGs failed within 30 days of first use in Europe/ANZ and in the United States.

Successful AVG use was less likely if located in the lower arm or among HD patients who were black or had peripheral vascular disease in logistic regression analyses restricted to the United States due to sample size limitations outside the United States (Table S4).

Time From Creation to First Successful Use of a Newly Created AV Access: DOPPS 4 and 5

Among newly created AVFs that were successfully used for 30 or more days in DOPPS phases 4 to 5, time until the first day of successful AVF use differed greatly by international region (Fig 2A), from a median of 10 (IQR, 2-15) days in Japan, 46 (IQR, 28-67) days in Europe/ANZ, and 82 (IQR, 57-116) days in the United States. Similar distributions were seen for AVFs located in the lower versus upper arm in each region (results not shown). Among newly created AVGs that were successfully used, time until the first day of successful AVG use differed considerably by region (Fig 2B), from a median of 6 (IQR, 1-15) days in Japan, 24 (IQR, 7-43) days in Europe/ANZ, and 29 (IQR, 16-48) days in the United States.

Discussion

Large international differences are demonstrated in the percentage of upper-extremity AVFs located in the lower arm, predictors of lower- versus upper-arm AVF location, successful AVF use, and time to first use of newly created AVFs and AVGs. Time trend analyses of AVF location from DOPPS phases 1 to 5 (1996-2015) indicated high use of lower-arm AVFs in Japan throughout these phases and intermediate use in Europe/ANZ from 77% in DOPPS phases 1 to 2 to ~65% in DOPPS phases 4 to 5. In contrast, lower-arm AVF use has declined more than 2-fold in the United States, from 70% in DOPPS phase 1 (1996-2001) to 32% in phase 5 (2012-2015). Similar

Table 2. Adjusted Odds Ratios of AVF Location (Lower vs Upper Arm) by Patient Characteristics and Study Region for All AVFs Created During the Study

Characteristic	OR (95% CI)		
	Japan (n = 807)	Europe/ANZ (n = 1,731)	United States (n = 1,709)
Male sex (vs female)	0.98 (0.59-1.61)	1.81 (1.46-2.23)	1.64 (1.33-2.04)
Black race (vs nonblack)	—	—	0.88 (0.69-1.13)
Age, per 5-y older	0.90 (0.79-1.01)	0.97 (0.94-1.00)	0.98 (0.95-1.02)
BMI, per 5-kg/m^2 greater	1.00 (0.69-1.44)	1.10 (1.00-1.22)	1.01 (0.94-1.09)
Cardiovascular disease (vs no)	0.81 (0.48-1.36)	1.01 (0.81-1.27)	0.99 (0.76-1.29)
Congestive heart failure (vs no)	0.62 (0.36-1.05)	0.84 (0.65-1.10)	0.81 (0.62-1.07)
Diabetes (vs no)	0.95 (0.57-1.60)	0.69 (0.55-0.86)	0.99 (0.77-1.28)
Peripheral vascular disease (vs no)	1.02 (0.51-2.04)	0.80 (0.63-1.02)	0.64 (0.46-0.90)
Dialysis vintage, per 1-y greater	0.94 (0.90-0.98)	0.92 (0.89-0.96)	0.86 (0.80-0.91)

Note: Separate models were run by region; each model was adjusted for study phase and for all characteristics shown in the table and accounted for patient clustering. Cardiovascular disease includes any coronary artery disease, cerebrovascular disease, or other cardiovascular disease. Overall N = 4,247.
Abbreviations: ANZ, Australia and New Zealand; AVF, arteriovenous fistula; BMI, body mass index; CI, confidence interval; OR, odds ratio.

international differences were seen in patients having a dialysis vintage less than 2 years in DOPPS phases 1 to 5. Even among younger males (aged < 55 years), <50% had AVFs located in the lower arm in the United States in DOPPS phases 4 and 5 compared with 73% in Europe/ANZ and 98% in Japan.

This finding should be of great concern for health care professionals and hemodialysis patients in the United States and raises questions concerning the long-term implications for relatively young HD patients for whom an AVF is created in the upper rather than lower arm. The implications are not only in limiting the number of available sites for creating future AVFs when needed, but whether these patients more likely will be relegated to a central venous catheter, and its complications, when AV access sites are exhausted. This exhaustion will come earlier due to the loss of multiple lower-arm AVF possibilities (eg, snuff box, distal, and midradiocephalic and Gracz-type fistulas). Other potential negative aspects of upper-arm AVFs are the higher frequency of steal syndrome and potential adverse long-term effects of high AVF blood flow on cardiac function.[11-14] Vascular access practice guidelines in the United States, Europe, and Japan have strongly recommended AVF placement in distal upper-extremity sites as the first choice for AVF creation when feasible.[1-4] This leads to the question of why AVF arm location has changed so dramatically in the past 1 to 2 decades in the United States. The timing and trend in this shift from lower- to upper-arm AVFs mirror the onset and uptake of the Fistula First Initiative.[15,16] This dramatic US shift in AVF arm location may have occurred in part from efforts and pressures to achieve higher AVF use rates in response to the Fistula First Initiative (particularly in switching from AVGs to AVFs), the Centers for Medicare & Medicaid Services Quality Incentive Program,[17] and contemporaneous studies reporting greater successful primary patency for AVFs placed in the upper versus lower arm.[18-24] In the current investigation, successful use was greater for upper- versus lower-arm AVFs created in US patients. However, in Europe/ANZ and Japan, there was no definitive indication that successful AVF use was inferior for lower- versus upper-arm AVFs. This suggests a

Table 3. Successful AVF Use, by Region and AVF Location, Among AVFs Created During Study Follow-up

	Japan			Europe/ANZ			United States		
	Overall	Upper Arm	Lower Arm	Overall	Upper Arm	Lower Arm	Overall	Upper Arm	Lower Arm
Among AVFs with ≥30 d of follow-up									
Total no. of created AVFs used in analysis	456	60	396	1,022	459	563	1,266	863	403
AVFs successfully used for ≥30 d	87%	82%	88%	67%	69%	65%	64%	67%	56%
Allowing up to 7 mo after AVF creation for successful AVF use[a]									
Total no. of created AVFs used in analysis	446	59	387	902	408	494	1,041	722	319
AVFs successfully used for ≥30 d	89%	83%	90%	76%	78%	74%	77%	80%	71%
AVFs never used within 7 mo of date created	8%	12%	7%	22%	21%	24%	22%	19%	28%
AVFs with some use but <30 d of use	3%	5%	3%	2%	1%	2%	1%	1%	1%

Notes: In United States, 8.7% of patients with an AVF created during the study had transferred to another hemodialysis facility after AVF creation, with most transfers occurring more than 6 months after AVF creation. The success rate for AVFs was essentially the same if these patients were excluded.
Abbreviations: ANZ, Australia and New Zealand; AVF, arteriovenous fistula.
[a]Required that each AVF have 30 or more days of follow-up.

Table 4. Hazard Ratios of Time From AVF Creation Until Successful Use by Cox Regression: Associations With Patient Characteristics by Study Region

Characteristic	HR (95% CI)		
	Japan (n = 456)	Europe/ANZ (n = 1,022)	United States (n = 1,266)
Male sex, vs female	1.01 (0.82-1.25)	1.32 (1.11-1.57)	1.38 (1.20-1.60)
Black race, vs nonblack	—	—	0.96 (0.82-1.14)
Age, per 5-y older	1.01 (0.97-1.05)	1.01 (0.98-1.04)	1.01 (0.99-1.04)
Dialysis vintage, per 1-y greater	1.00 (0.99-1.02)	1.01 (0.99-1.02)	0.99 (0.96-1.02)
BMI, per 5-kg/m^2 greater	1.02 (0.87-1.19)	0.93 (0.87-1.00)	1.00 (0.95-1.05)
Cardiovascular disease, vs no	1.07 (0.87-1.32)	0.81 (0.68-0.96)	1.02 (0.84-1.23)
Congestive heart failure, vs no	0.95 (0.77-1.18)	1.20 (0.99-1.46)	0.96 (0.79-1.15)
Diabetes, vs no	1.05 (0.85-1.29)	0.93 (0.78-1.11)	0.92 (0.78-1.10)
Peripheral vascular disease, vs no	0.89 (0.69-1.16)	1.10 (0.92-1.31)	0.99 (0.79-1.25)
Facility % fistula use, per 5% greater	1.03 (0.99-1.08)	1.04 (1.01-1.07)	1.00 (0.96-1.04)
Facility median blood flow rate, per 20-mL/min greater	0.98 (0.90-1.08)	0.96 (0.91-1.01)	1.02 (0.99-1.06)
Upper arm, vs lower arm	0.73 (0.56-0.96)	1.00 (0.85-1.17)	1.29 (1.11-1.50)

Notes: Cox regression providing the HRs of successful AVF use for each study region for AVFs created during follow-up in DOPPS 4 and 5; each model was stratified by study phase, adjusted for all characteristics in table, and accounted for patient clustering. Cardiovascular disease includes any coronary artery disease, cerebrovascular disease, or other cardiovascular disease. Overall N = 2,744. HR > 1.0 indicates shorter time to successful AVF use or greater AVF use.
Abbreviations: ANZ, Australia and New Zealand; AVF, arteriovenous fistula; BMI, body mass index; HR, hazard ratio.

selection bias in the United States to succeed with larger vessels in the first attempt. In contrast, practitioners in Japan and Europe/ANZ may delay using upper-arm vessels until after lower-arm fistula(5) have failed, with comorbid conditions ultimately accruing their effects upon upper-arm vessels, resulting in similar lower- versus upper-arm AVF success in Japan and Europe/ANZ. Greater routine use of preoperative vascular ultrasound during the past 15 years may partially account for some of the switch in the United States from lower- to upper-arm AVF placement. However, comparable use of ultrasound is seen in western European HD units (R Pisoni, DOPPS phase 4, unpublished results), and yet a much smaller shift from lower- to upper-arm AVF placement is seen in Europe than the United States. Moreover, a randomized trial of routine preoperative vascular ultrasound versus physical examination only for AVF construction[25] showed no significant difference in forearm versus upper-arm placement (~61%) of new AVFs in the 2 treatment groups.

Table 5. Successful AVG Use by Region Among AVGs Created During Study Follow-up

	Japan	Europe/ANZ	US
Among AVGs with ≥30 d of follow-up			
Total no. of created AVGs used in analysis	133	251	594
AVGs successfully used for ≥30 d	86%	75%	78%
Allowing up to 3 mo after AVG creation for successful AVG use[a]			
Total no. of created AVGs used in analysis	130	242	564
AVGs successfully used for ≥30 d	89%	78%	83%
AVGs never used within 3 mo of date created	5%	17%	15%
AVGs with some use, but <30 d of use	5%	6%	3%

Abbreviations: ANZ, Australia and New Zealand; AVG, arteriovenous graft; US, United States.
[a]Required that each AVG have ≥30 days of follow-up.

In Japan, 90% of HD patients dialyze with an AVF[5] and yet display higher successful use of newly created AVFs (Table 1) and higher cumulative AVF survival rates than in North America and Europe/ANZ[6] despite ~90% of AVFs located in the lower arm among Japanese HD patients. We do not know all the reasons that Japanese practitioners attain such high levels of successful AVF use, but the following observations are pertinent: a much lower median blood flow rate is used in Japan (200 mL/min) than in the United States (425 mL/min) and Europe/ANZ (300 mL/min). Lower blood flow rates are feasible in Japan due to smaller body weight and longer median treatment time (Japan: 240 minutes; United States: 215 minutes) in achieving fairly comparable mean single-pool Kt/Vs (Japan: 1.5; United States: 1.6; year 2015, DOPPS, unpublished results). Furthermore, prior unpublished DOPPS work has found much greater use of smaller gauge needles for carrying out HD with an AVF in Japan versus the United States.

These practice differences, in combination with excellent surgical technique, may be key factors resulting in ~90% successful use of newly created AVFs in Japan, with a median time of 10 days to first successful AVF use and with the great majority of these AVFs placed in the lower arm, despite Japanese HD patients having an older mean age than US or Europe/ANZ patients (Table 1). The great majority of Japanese HD patients (91%) dialyze with an AVF versus 68% in the United States.[5] Thus, patient selection for type of access to be given is a relatively minor issue in Japan compared with other countries, and the prevalence of diabetes among Japanese HD patients is intermediate between that of US and Europe/ANZ HD patients. The slightly lower successful use of upper- versus lower-arm AVFs seen in Japan may be a reflection that

upper-arm AVFs may be relegated to patients with poor vasculature compared with patients receiving a lower-arm AVF, particularly given that upper-arm AVFs are rarely used in Japan and thus are possibly reserved for patients having poor options for distal arm AVF creations or in whom prior forearm AVFs have failed. In contrast, in the United States, based on trend analyses, upper-arm AVF placements may be more of an indication of a practice preference and not as tightly linked to the quality of a patient's vasculature as in Japan.

DOPPS results for the United States are similar to the 64% successful AVF use reported for the United States in the 2016 US Renal Data System (USRDS) Annual Data Report for incident patients in 2013.[26] The median time to the first day of successful AVF use for the United States in DOPPS is shorter than the median of 112 days reported by the USRDS for incident HD patients,[26] with the latter calculated from the AVF creation date until end of the first month's reported use, which possibly overestimates maturation time by about 15 days on average. Within each international region, distributions of time until first successful AVF use were similar for AVFs located in the lower versus upper arm. Altogether, our findings suggest that time to first successful AVF use may be more relevant to dialysis-related practice than AVF characteristics. It is noteworthy that the observed practice in Japan for time to first AV access use is shorter than recommended by Japanese guidelines, which recommend a first puncture time of more than 2 weeks after AV access creation.[2]

The current investigation informs the scarcely described topic of international AVG creation and successful use. Successful AVG use observed for the United States in DOPPS is consistent with that reported in the Dialysis Access Consortium Trial,[27] although end points were defined somewhat differently. Early failures were considerably more common for newly created AVGs versus AVFs in the current work.

A strength of the current study is its representative nature to reflect real-world practice across many dialysis units in each country (rather than selected academic HD units). However, a limitation is the dependence on accurate reporting of vascular access data from each study site in this observational study design.

Large international differences exist in the percentage of arm AVFs created in the lower arm, predictors of lower- versus upper-arm AVF location, successful use of newly created AVFs, and time to first use of newly created AVFs and AVGs. These findings, coupled with large differences in AVF survival across these international regions, raise important questions regarding what is best practice and how it is best achieved to optimize vascular access outcomes. Importantly, the large shift in predominantly lower- to upper-arm AVF creation in the United States, even in "ideal" young patients for AVF creation, raises the question of whether this practice shift may place patients at greater risk for exhausting available sites for future AVF creation when needed. This could have substantial health implications for patients and economic implications for health care systems.

Supplementary Material

Figure S1: Facility distribution of AVF location in lower arm, by region.

Figure S2: Percentage of new AVFs located in lower arm in HD patients by age group, for new AVFs created on or before 2 y of HD.

Table S1: Characteristics of study patients at enrollment with a newly-created AVF vs AVG, by DOPPS country, and by AVF access location.

Table S2: Association between patient characteristics and successful AVF use, by region, with increasing levels of covariate adjustment, among AVFs created during follow-up.

Table S3: Association between patient characteristics and successful AVF use, by region, among AVFs created during follow-up, and allowing up to 7 mo for successful AVF use.

Table S4: Association between patient characteristics and successful AVG use among AVGs created during follow-up, and allowing up to 3 mo for successful AVG use; US only.

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