

Vascular Access Surgery Managed by Renal Physicians: The Choice of Native Arteriovenous Fistulas for Hemodialysis

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● **Background:** After decades of success in dialysis research and treatment, prompt availability of a well-functioning vascular access for dialysis remains a disturbing problem. On the basis of a single-center experience in which nephrologists are responsible for access surgery, we sought to identify predictors of catheter use at the start of hemodialysis (HD) therapy and risk factors affecting first permanent access survival. **Methods:** Demographics, comorbid conditions, predialysis follow-up, and access-related procedures of the 197 consecutive patients beginning extracorporeal treatment between 1995 and 2001 were prospectively entered into our database. **Results:** Despite the high prevalence of comorbidities (diabetes, 22%; cardiovascular disease, 50%; neoplasm, 15%), all subjects received a native fistula as a first permanent access, but almost 60% initiated HD therapy using a catheter. The latter showed more comorbidities and were referred later. According to the Kaplan-Meier method, median primary and secondary survivals of the first fistula were 38.1 months and more than 70 months, respectively. The Cox model indicated that diabetes and previous catheter use were independently associated with 85% and 63% greater relative risks for first failure, but only diabetes led to a greater risk for final failure (relative risk, 2.38; $P = 0.05$). **Conclusion:** Both the absence of predialysis care and presence of comorbidity influence access type at HD therapy initiation and fistula survival. Earlier intervention strategies can increase the use and durability of a native fistula for HD. Direct involvement of nephrologists in the management of access surgery can be helpful in this respect. *Am J Kidney Dis* 40:1264-1276.

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INDEX WORDS: Vascular access (VA); hemodialysis (HD); end-stage renal disease (ESRD); predialysis care.

DESPITE CONTINUOUS advances in dialysis technology, vascular access (VA) to the circulation is still the Achilles' heel of long-term hemodialysis (HD) therapy.¹ Creation and maintenance of a functioning VA absorb increasing health care resources, whereas VA complications account for up to 25% of hospital admissions, represent 15% to 20% of total Medicare expenditures for the end-stage renal disease (ESRD) population, and disproportionately affect patients who are older, women, and black and/or those with diabetes.²

The autologous arteriovenous fistula (AVF) developed by Kenneth Apple in New York in the early 1960s is still the first-choice (primary) VA for patients with ESRD treated with HD therapy.³ The radiocephalic AVF at the wrist (distal AVF) and upper-arm AVF (proximal AVF) offer an easily repeated and durable access to the circula-

tion that is less subject to major complications than other VAs, such as arteriovenous grafts (grafts) or temporary or permanent central venous catheters (catheters).⁴ Furthermore, both primary and secondary patency rates of AVFs have been reported to be greater than those of grafts, even in facilities in which grafts are preferred.⁵⁻⁹ For these reasons, the National Kidney Foundation-Dialysis Outcomes Quality Initiative¹⁰ guidelines recommend AVFs as the first-choice or primary VA for HD therapy.

Nevertheless, there is considerable geographic variation in the distribution of type of VA used among prevalent patients with ESRD in industrialized countries, which not only reflects different degrees of access to tertiary care for renal patients and different reimbursement strategies penalizing AVF construction, but also potentially affects HD outcomes. Although the prevalence of patients with an AVF is high (60% to 80%) in Canada, Japan, and Europe, AVFs account for only 21% to 28% of VAs in use in the United States, where more than 50% of patients have grafts, and permanent catheters are widely used.^{1,11}

The high prevalence of temporary catheter use at the start of HD therapy also is worth noting because of its possible impact on AVF survival and HD morbidity and mortality. This was as great as 68% in a cohort of 356 American pa-

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tients, whereas early referral was associated significantly with a greater probability of having an AVF when starting HD therapy after adjusting for other variables and comorbid factors.⁴ For this reason, timely preparation for dialysis therapy is one of the main objectives of any predialysis program, and treatment access surgery is crucial. However, there is little recent literature concerning single-center experiences of VA surgery, particularly performed by renal physicians.¹² Earlier studies of VA survival are less representative of current patients and practices because they date from a period when the ESRD population was younger and had fewer comorbidities.

To implement quality assurance covering VA issues, we developed a database to monitor a series of outcome variables and measures with the aim of improving VA management and optimizing each step of the access-placement process, from preoperative investigations and vessel selection to surgical techniques and surveillance strategies.

Purposes of this study are to: (1) establish the prevalence of comorbid conditions and cardiovascular risk factors among patients new to HD therapy who received an AVF created by renal physicians at our center, (2) identify predictors of VA type (temporary catheters or permanent accesses) at the start of HD therapy, (3) evaluate survival of the first permanent VA, and (4) evaluate the impact of catheter use on dialysis adequacy.

PATIENTS AND METHODS

Study Design

This longitudinal cohort study examined VA outcomes of all patients with ESRD who started HD therapy (defined as any kind of extracorporeal treatment) at our center between January 1, 1995, and December 31, 2001. HD is the prevalent first renal replacement modality for incident patients with ESRD at our center (62% versus 38% on peritoneal dialysis [PD] therapy). Patients switched from PD therapy (defined as any kind of peritoneal technique), but without a previous history of HD therapy, also were considered. All patients gave their informed consent.

Inclusion criteria were starting HD therapy for ESRD with the creation and management of a first VA by renal physicians. Exclusion criteria were previous history of HD and kidney transplantation (because patients with a previous failed permanent VA are less likely to receive a primary VA and are at greater risk for VA failure and death) and an incomplete follow-up or exit from the system to see other caregivers. Patients who transferred to other dialysis units after entering the study were censored because follow-up

information had to be prospectively captured and verified within our center.

VA Database and Data Sources

For the purpose of this study, we prospectively collected data concerning patient demographics, risk factors, underlying renal disease and comorbidities, HD prescription, and VA surgery, including VA type and site, date and description of the intervention, VA complications, catheter type and site, and date of first use. To measure patient exposure to renal care, their predialysis follow-up was evaluated on the basis of frequency of visits to a nephrology center rather than the interval between first referral to a renal specialist and start of dialysis therapy. Follow-up before ESRD was defined as absent (no predialysis care), present (fewer than three nephrologist visits per year), or intense (three or more visits per year). Because a high-intensity index may not be associated with a greater likelihood for timely placement of a VA if patients were not seen by a nephrologist during the 2 to 6 months preceding dialysis therapy, the interval between the last visit and start of HD therapy initiation also was considered.

Data entered into a central database for analysis were obtained from the following sources: the unit's surgery registry, the unit's catheter registry, HD patients' medical records with all discharge summaries, clinical charts of all first HD-related hospitalizations, nursing HD flow sheets, hospital electronic database of admissions and discharges (with diagnosis-related group classification and *International Classification of Diseases, Ninth Revision*), and hospital electronic database of department costs (with a description of materials and medications). The database was continuously updated by recording all VA-related procedures and such events as death, transplantation, transfer to another unit or PD therapy, and catheter placement and removal.

Risk Factors and Comorbid Conditions

Variables considered for analyses were demographics (age, sex), cardiovascular risk factors and comorbid conditions (smoking habit, body mass index, dyslipidemia, diabetes, arrhythmia, heart failure, peripheral and cerebral vasculopathy, coronary artery disease, hypertension, and neoplasm). Patients were considered to have cardiovascular disease if they had a documented diagnosis of congestive heart failure or ischemic heart disease caused by coronary artery disease with or without myocardial infarction; arterial hypertension was considered a risk factor when known for at least 5 years.

Patients were considered to have diabetes if they had been administered oral antidiabetic drugs or insulin after a previously documented diagnosis of diabetes mellitus. They were considered to have peripheral or cerebrovascular disease if clinical and instrumental findings were available, including claudication, stroke, transient ischemic attack, or documented ultrasound or angiographic abnormal results. They were considered to have a neoplasm when a clear diagnosis had been made, and considered to be smokers if they had ever smoked.

Diagnostic Protocol, Surgical Technique, and Catheter Placement

Two nephrologists on our team are responsible for creating VAs and implementing catheters. They had placed VAs for 11 to 16 years before the start of the present study and shared experiences with other access surgeons.

All patients in this cohort underwent a preoperative clinical examination of arm arteries (inspection, palpation, and auscultation, with bilateral blood pressure measurement) and veins using outflow occlusion by means of a tourniquet. Vascular mapping of the arm was performed regularly before surgery if the patient had previously undergone superior cava vein catheterization, had a previous AVF dysfunction (in the case of revisions), or no vein was apparent. An echo-power-Doppler was supported by a venogram, if indicated.

Site and type of VA were chosen mainly on the basis of clinical examination, and all interventions were performed under local anesthesia. To increase the use of native AVFs, we prepared a standard autogenous AVF at the distal lateral wrist (radiocephalic anastomosis) and the antecubital fossa of the elbow (radiocephalic and brachiocephalic or, less frequently, brachio basilic anastomoses), starting distally with the nondominant arm to preserve proximal sites. The vein usually was prepared by dilatation and gently washed with heparinized saline (20 UI/mL). Distal AVF anastomoses were both side to side and end to side, and proximal anastomoses were mainly side to side, with arteriotomies of 6 to 7 and 4 to 5 mm, respectively. In comparison to other series,¹³⁻¹⁶ use of the perforating vein was rare, as was transposition of basilic veins. We give absolute priority to native vessels; this limits the use of grafts, but when needed, they are prepared using a subcutaneous polytetrafluoroethylene loop placed in the forearm.

When necessary, temporary catheters (uncuffed, untunneled, double-lumen type) were inserted in both the inferior (femoral vein cannulation) and superior cava vein (internal jugular vein cannulation) systems on both sides, whereas all permanent catheters (cuffed, tunneled, dual-lumen or twin single-lumen types) were inserted only in the right (mainly) or left internal jugular vein.

Event and Efficacy Measures

Deaths were divided into all-cause (overall mortality) and specific-cause deaths (cardiovascular, infections, neoplasm, others).

A VA was considered patent if it worked well after the intervention and was capable of providing blood flow (Q_B) sufficient to obtain an adequate dialysis dose within a maximum of 5 h/session. VA failure was defined as definitive clotting or malfunction caused by stenosis or partial thrombosis, usually suspected on the basis of inflow monitoring and dynamic pressure measurements and ascertained by recirculation studies, echo-power-Doppler, and fistulography, if necessary. This was the primary end point of the study, and if it occurred during the first 7 days after VA creation, it was considered an early failure.

Failure to mature in the absence of these complications also was considered an early failure. A new intervention usually was performed within 1 week of the event (0 to 5

days). We distinguished a VA revision (restoring patency of the same VA) from a new creation, the former without and the latter with a change in VA conduit (new AVF location or VA type). Depending on the site and extension of stenosis or organized thrombosis, a revision with the creation of a new shunt just upstream from the previous one or a surgical, pharmacomechanical (thrombolysis without devices), or percutaneous radiological intervention (angioplasty, not practiced in this cohort) for recent thrombosis could be performed.

Accordingly, primary survival was defined as the time from VA creation to first failure (intervention-free period), and cumulative (unassisted) primary patency, as the percentage of all VAs at risk at any one time that were still functioning without an intervention. Secondary survival was defined as the time from VA creation to the time it could no longer be used for dialysis, regardless of the number of revisions required to maintain patency (final failure), and cumulative (assisted) secondary patency, as the percentage of all VAs at risk at any one time that were still functioning, including all revisions and until a new creation or switching to catheter or PD therapy. Life expectancy was defined as the median value for secondary survival. Given the main objectives of the study, our analysis concentrated on survival of the first AVF of patients starting HD therapy because considering combined survival of all VAs would have multiplied the total number of observations and included some patients and their related risk factors and comorbidities more than once.

Dialysis adequacy was measured by means of equilibrated dialysis index ($eqKt/V$; after 30 minutes) using the urea kinetic model-single pool variable volume (UKM-SPVV),¹⁷ with dialyzer clearance (K) and urea distribution volume (V) modeled on patient data. Q_B values after 1 and 3 months were recorded by dialysis monitors. Q_B and Kt/V were considered secondary outcome measures and indirect means of monitoring VA dysfunction.

Statistical Methods

Baseline characteristics and predictors of AVF use. Mean values and frequencies were compared using analysis of variance, *t*-test, or chi-square test, as appropriate. Logistic regression was planned to evaluate the statistical association between the selection of a distal or proximal AVF as a first approach and patient characteristics, cardiovascular risk factors, comorbidities, previous use of temporary central venous catheters, and previous PD therapy. Logistic regression also was used to test the association between availability of a functioning fistula at the start of dialysis therapy and patient characteristics, intensity of predialysis care, and presence of a visit during the 2 to 6 months preceding the start of HD therapy.

Access survival analysis. Univariable analysis of the primary survival of the first AVF was described using the Kaplan-Meier technique, with date of AVF failure as the end point. Patients were censored when they were switched to PD therapy, transferred to another dialysis unit, received a kidney graft, or on the final observation date (December 31, 2001) if they had a functioning AVF. Patients who died of any cause also were censored. Cox proportional hazard regression models were used to compare time to event

according to a set of risk factors. Models were stratified on the basis of the distal or proximal location of the AVF. Risk factors related to patient demographics and comorbid conditions, as well departmental organizational issues (eg, surgeon, early versus late referral, previous PD therapy), also were considered. Patients were censored as in the descriptive analysis. The proportionality of covariates was evaluated using log minus log plots. Analysis was performed twice, with and without early failures.

Secondary patency was evaluated as in primary patency (including early failures), but the event was defined as the need to create a new VA in the upper arm on the same side (when the first VA was distal) or in the other arm. Survival was censored as in the previous model.

Revision rate was calculated with time at risk defined as time until the event or time of censoring.

All statistical analyses were performed using SPSS software, version 10.1 (SPSS Inc, Chicago, IL). The contribution of covariates to explain the dependent variable was assessed by means of a two-tailed likelihood ratio test, with *P* less than 0.05 considered significant.

Estimated relative risks and their 95% confidence intervals (CIs) are reported for all variables retained in regression models.

RESULTS

Baseline Characteristics, Referral Patterns, and Patient Survival

In accordance with selection criteria, 197 patients (mean age, 65.7 ± 13.0 years; median, 67.6 years) who underwent AVF construction and started HD therapy at our center between January 1995 and December 2001 were evaluated. Twenty-nine patients (14.7%) had been treated previously with PD therapy for a median duration of 14.7 months (range, 0.1 to 54.4 months). The population included 117 men (59.4%), and 57.9% were elderly (age ≥ 65 years). There were 43 patients with diabetes (21.8%), who were not significantly older than subjects without diabetes (mean age, 68.4 versus 64.9 years). Table 1 lists underlying renal diseases, cardiovascular risk factors, and considered comorbid conditions. Excluding arterial hypertension (present in almost 87% of patients), only 74 patients (37.6%) had no comorbidity (cardiovascular disease, diabetes, neoplasm, or chronic lung disease).

In terms of predialysis care, 73 patients (37.1%) had never seen a renal specialist, 79 patients (40.1%) had been examined up to twice per year, and 45 patients (22.8%) had been followed up more intensively. Eighty-two patients (41.6%) had been referred to a renal physician more than 1 year before ESRD, whereas 96 patients (48.7%)

Table 1. Description of Underlying Renal Disease and Cardiovascular Risk Factors and Comorbidities

Renal disease	
Unknown	7 (3.6)
Glomerulonephritis	23 (11.7)
Interstitial nephritis	36 (18.3)
Hereditary disease	22 (11.2)
Vascular disease	73 (37.1)
Systemic disease	30 (15.2)
Other	6 (3.0)
Total	197 (100)
Cardiovascular risk factors/comorbidities	
Age > 65 y	114 (57.9)
Overweight*	39 (19.8)
Hypertension	171 (86.8)
Hypercholesterolemia†	67 (34.0)
Hypertriglyceridemia†	88 (44.7)
Diabetes	43 (21.8)
Chronic lung disease	23 (11.7)
Heart failure	27 (13.7)
Arrhythmia	17 (8.6)
Vasculopathy	91 (46.2)
Cardiovascular disease	99 (50.3)
Systemic disease	10 (5.1)
Smoking habit	66 (33.5)
Neoplasm	30 (15.2)

NOTE. Values expressed as number (percent). Normal range of values for body mass index* and lipid profile† from.^{18,19}

had seen a nephrologist during the 2 to 6 months before the start of HD therapy. Only 13.5% of these patients had no previous follow-up, and only 17% of those without previous care compared with 60.7% and 77.7% of those with follow-up present or intense were seen in this interval (*P* < 0.001). Patients referred later and less intensely followed up had a greater proportion of comorbid conditions (72% versus 53.3%; *P* = 0.02). This difference also was observed after patients were stratified on the basis of the presence or absence of a nephrologist visit during the 2 to 6 months preceding dialysis therapy.

Overall mean follow-up of the cohort as a whole was 20.4 months, for a total of 335 patient-years. During follow-up, 16 patients underwent transplantation, 3 patients were switched to PD therapy, 11 patients were transferred to other dialysis units, and 78 patients died (6 patients, during the first month). No patient was referred to another center for VA surgery. Considering only patient time spent on HD therapy, the mortality rate was 22.7 deaths/100 patient-years. Causes of death were cardiovascular events,

57.7%; infections, 16.6%; and neoplasms, 12.8%. Median patient survival was 41.9 months (95% CI, 31.1 to 52.7), and cumulative survival rates at 12, 24, and 48 months were 75%, 65%, and 41%, respectively. Median patient survival by location of AVF and the presence or absence of diabetes is listed in Table 2 (univariate analysis). After stratifying for diabetes²⁰ and adjusting for age, site of the AVF no longer correlated significantly with patient survival ($P = 0.14$).

VA Surgery

Creation of a native AVF was attempted in all cases by two renal physicians who had undergone specific long-term training and who were responsible for 55.3% and 44.7% of interventions. Including 28 revisions, this incident population underwent 309 operations (197 first and 112 subsequent interventions); 209 operations in the forearm and 100 operations at the elbow, including 11 graft bridge constructions or revisions. First and subsequent interventions are shown in Fig 1: 81.2% of the patients received a distal AVF in the first operation.

There were no more than two revisions per VA. In the case of first VAs, 20 patients (10.2%) underwent a revision of the first AVF (0.10 per patient; 16 distal and 4 proximal AVFs). The remaining 177 patients (89.8%) underwent only one surgical intervention. There was no significant difference in revision rates for distal and proximal AVFs (10% versus 10.8%), whereas there was a highly significant difference in distribution of revisions between patients who experienced an early failure and the others (33% [$n = 8$] versus 6.9% [$n = 12$]; $P < 0.001$). Seven revisions were required for the third intervention (6 distal and 1 proximal AVF), and one revision (a graft) for the fourth intervention. The rest of the VA surgery contributed to the preparation of new VAs. During follow-up of the first AVF,

there were 0.074 revisions per patient-year at risk, with more involving proximal than distal AVFs (0.130 versus 0.067) and patients with versus without diabetes (0.178 versus 0.056). The revision rate during follow-up as a whole was 0.083, an average of one revision every 12 years.

Among the prevalent HD population of our center as of December 31, 2001 ($n = 118$), 87% of patients ($n = 89$) had an AVF, 2% had a graft, and 11% used a catheter. Table 3 lists morbidity related to all 309 VA procedures.

Characteristics of patients by AVF type are listed in Table 4. Patients who received a distal AVF were more likely to be men, younger, taller, and heavier. Logistic regression confirmed a significant predictive role of only age on choice of location ($P = 0.015$) because the odds ratio (OR) for a proximal AVF was 1.04/y (95% CI, 1.013 to 1.069), whereas female sex retained its borderline association with proximal AVFs ($P = 0.06$).

Type of VA at the Start of HD Therapy

At the start of HD therapy, 117 patients (59.7%) had a temporary catheter and the others had an AVF. Among those who began therapy using a temporary VA, 39 patients (33.3%) had already undergone VA surgery; 67 patients (57.3%) did so during the first month of HD, and 11 patients (9.4%) thereafter. Patients who started HD therapy with a catheter used their fistula significantly earlier (median maturation time before needling, 23 versus 32 days; $P = 0.01$).

There was no significant difference in distribution of demographic data, risk factors, and considered comorbidities by VA type at the start of HD therapy. Conversely, type of predialysis follow-up significantly predicted the presence of an AVF, with prevalences of patients who had a temporary catheter at the start of HD therapy of 86.1% in the group with no previous follow-up, 46.8% in patients who had received previous care, and 40.0% in the group with intense follow-up. Patients who started HD therapy using a catheter had a mean yearly nephrologist visit number of 1.14 versus 2.11 for those starting therapy with an AVF ($P < 0.001$), and the proportion was significantly greater in those who were not seen by a nephrologist during the 2 to 6 months before dialysis therapy (99% versus 14.5%; $P < 0.001$). On the basis of the logistic

Table 2. Crude Median Patient Survival According to Kaplan-Meier by Location of First AVF and Presence or Absence of Diabetes by Log-Rank Test

Condition	Months	95% CI	<i>P</i>
Patients with distal AVF	45.7	36.5-54.9	—
Patients with proximal AVF	24.6	14.8-49.8	0.001
Absence of diabetes	45.7	36.8-54.6	—
Presence of diabetes	20.9	8.20-33.5	0.004

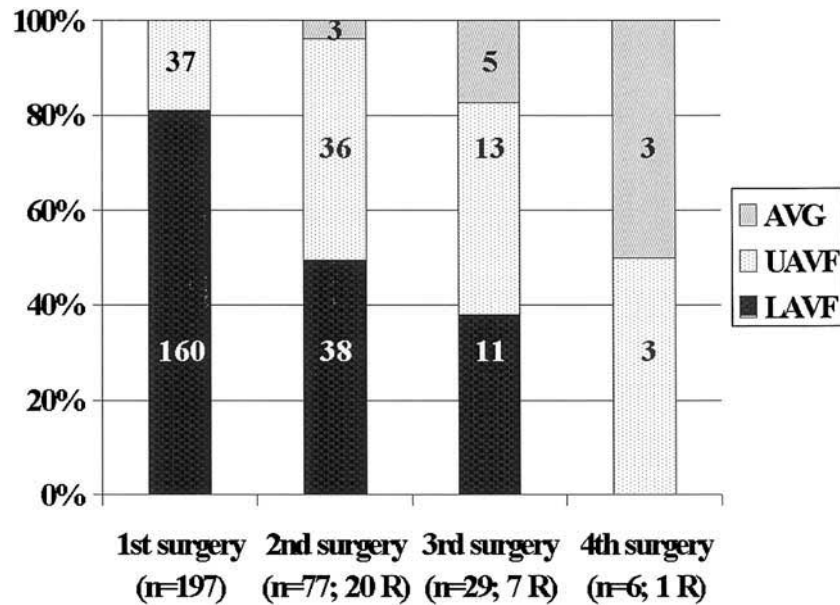


Fig 1. VA at first and subsequent surgery (including revisions [R]). Abbreviations: AVG, graft bridges; UAVF, upper AVF; LAVF, lower AVF.

regression model using the presence or absence of an AVF at the start of HD therapy as a binary outcome variable, there was a significantly increased risk for having a catheter in the presence of any comorbidity (OR, 2.24; $P = 0.019$), whereas both previous PD therapy (OR, 0.35; $P = 0.03$) and predialysis care (present and intense versus no care, ORs, 0.12 and 0.11, respectively; $P < 0.001$) had a protective effect. When the presence of a nephrologist visit during the 2 to 6 months preceding HD therapy was entered into the model, all other covariates lost their predictive power (Fig 2).

Primary and Secondary Patency of the First AVF

Median primary survival of the first AVF, including early failures and those that failed to mature, was 38.1 months (95% CI, 32.7 to 43.3).

Table 3. Morbidity of 309 VA Surgical Procedures, Including Revisions

Complications	Frequency	Proportion (%)
None	297	96.1
Aneurysm (revision)	2	0.6
Steal (conservative)	2	0.6
Steal (ligation)	4	1.4
Significant hematoma or bleeding	3	1
Infection (removal)	1	0.3
Total	309	100

Reanalysis after zeroing survival of the AVF that failed early showed that median survival was longer than 56 months. Cumulative survival after 6, 12, 24, and 36 months is listed in Table 5. In both models, primary survival of the first distal and proximal AVF was not significantly different. On the basis of log-rank statistics, factors predicting worse AVF survival were diabetes ($P = 0.03$), presence of a neoplasm ($P = 0.04$), need to start dialysis with a catheter ($P = 0.03$), and, at borderline levels, absence of pre-HD care ($P = 0.06$) and age older than 65 years ($P = 0.07$). When early events were set to zero, only diabetes proved to be a significant risk factor for shorter survival ($P = 0.02$). Finally, the stepwise Cox proportional hazard model showed that the presence of diabetes and, marginally, need for a previous catheter were independently associated with 85% and 63% greater relative risks for failure. The effect of diabetes also was confirmed when the 24 patients with early failure or an AVF that failed to mature were excluded, whereas the association between need for a previous catheter, although not statistically significant, maintained its effect. Results of multivariable analysis are shown in Fig 3.

Life expectancy of the first AVF was longer than 70 months, with no difference by VA location. The likelihood of secondary survival was greater than that of primary survival and reached

Table 4. Patient Characteristics, Cardiovascular Risk Factors, and Comorbidities by Type of AVF

Variable	Distal AVF	Proximal AVF	P
No. of patients	160	37	—
Surgeon A (%)	56.9	48.6	NS
Surgeon B (%)	43.1	51.4	NS
Age (y)	64.6 ± 13.1	70.4 ± 11.8	0.013
Male sex (%)	62.5	45.9	0.094
Height (cm)	165.7 ± 9.9	160.49 ± 8.19	0.003
Body weight (kg)	67.88 ± 15.58	61.88 ± 11.28	0.028
Body mass index (kg/m ²)	24.6 ± 4.6	23.9 ± 3.8	NS
Smoking habit (%)	35.6	24.3	NS
Triglycerides (mg/dL)	204 ± 152	186 ± 110	NS
Cholesterol (mg/dL)	200 ± 50	197 ± 48	NS
Hypertension (%)	88.1	81.1	NS
Diabetes (%)	20.0	29.7	NS
Chronic bronchitis (%)	10.0	18.9	NS
Heart failure (%)	12.5	18.9	NS
Previous peritoneal dialysis (%)	23	6	NS
Arrhythmia (%)	7.5	13.5	NS
Vasculopathy (%)	45	51.4	NS
Neoplasm (%)	13.1	24.3	NS

NOTE. Conversion factors for SI units for triglycerides (mg/dL to mmol/L), 0.0113; and for cholesterol (mg/dL to mmol/L), 0.0259.

Abbreviation: NS, not significant.

the level of statistical significance at 3 years ($P = 0.03$). On the basis of log-rank statistics, there was no difference in survival between distal and proximal AVFs by any of those covari-

ates. Again, the Cox proportional regression model showed that presence of diabetes was still independently associated with a more than double relative risk for failure, although the 95% CI

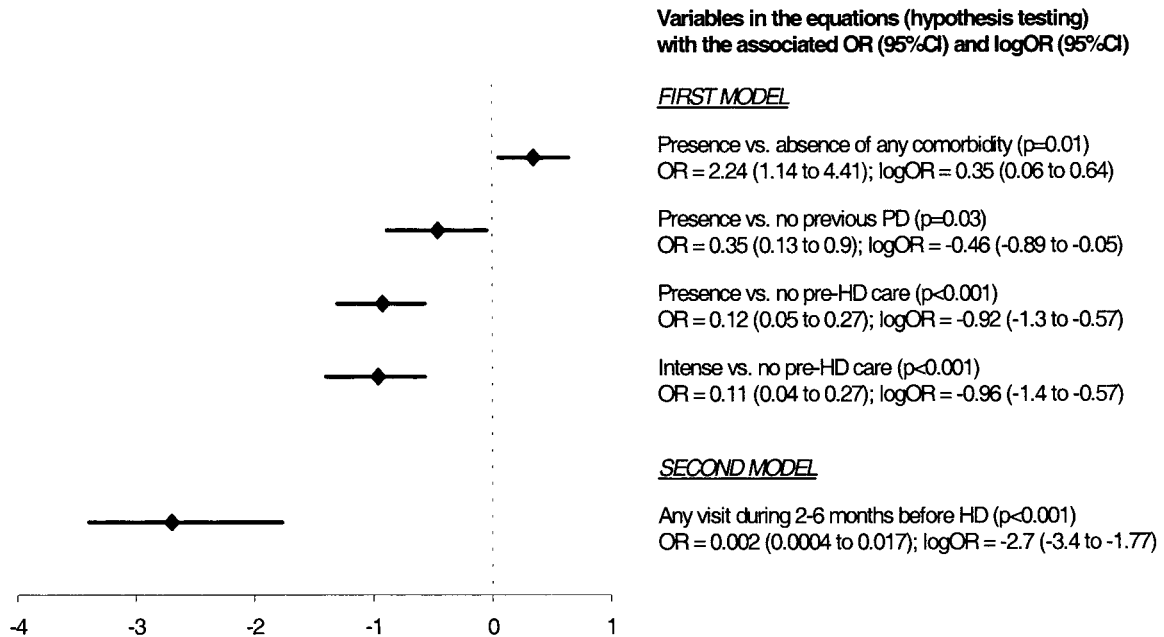


Fig 2. Logistic regression shows factors associated with the use of a temporary catheter at the start of HD. ORs expressed using a logarithmic scale.

Table 5. Primary and Secondary Patency Rates by AVF Type

	First AVF Patency Rates (%)			
	6 Mon	12 Mon	24 Mon	36 Mon
Primary patency including EF				
All AVFs	72	64	55	52
Distal AVFs	71	62	55	52
Proximal AVFs	74	69	48	44
Primary patency excluding EF				
All AVFs	76	70	61	58
Distal AVFs	76	70	61	59
Proximal AVFs	80	71	52	46
Secondary patency				
All AVFs	76.5	72	64	62
Distal AVFs	76	71	64	60
Proximal AVFs	80	73	73	73

NOTE. Primary patency results are shown by model. Abbreviation: EF, early failure.

around this estimate overlapped the zero difference point (Fig 3). Table 5 lists cumulative primary and secondary patency rates, and Fig 4 shows primary and secondary Kaplan-Meier survival curves of the first AVF.

Secondary Outcome Measures

Q_{BS} of all VAs were evaluated after 1 and 3 months, and delivered $eqKt/V$ was calculated after 3 months. One-month Q_{BS} were available for 126 AVFs and 62 temporary catheters (6 patients had died earlier, and 3 patients had been switched to PD therapy). There was a highly statistically significant difference ($P < 0.001$) in mean Q_B of 280 ± 35.6 versus 251 ± 56.1 mL/min between AVFs and temporary catheters (mean difference, 28.6 mL/min; 95% CI, 15.3 to 41.93, respectively). Three-month Q_{BS} were available for 159 AVFs and 10 permanent catheters (18 patients had died, and 10 patients had a temporary catheter insertion); 293.8 ± 28.5 mL/min in the former and 290 ± 31.6 mL/min in the latter. This difference was not statistically significant. In terms of HD treatment adequacy measured by means of $eqKt/V$ after 3 months, patients with catheters received a significantly lower dialysis dose (mean difference in $eqKt/V$, 0.10; 95% CI, 0.004 to 0.2; $P = 0.04$). Mean dose was 1.14 ± 0.16 in patients with an AVF and 1.04 ± 0.16 in those with a permanent catheter. There was no difference in adequacy parameters between distal and proximal AVFs.

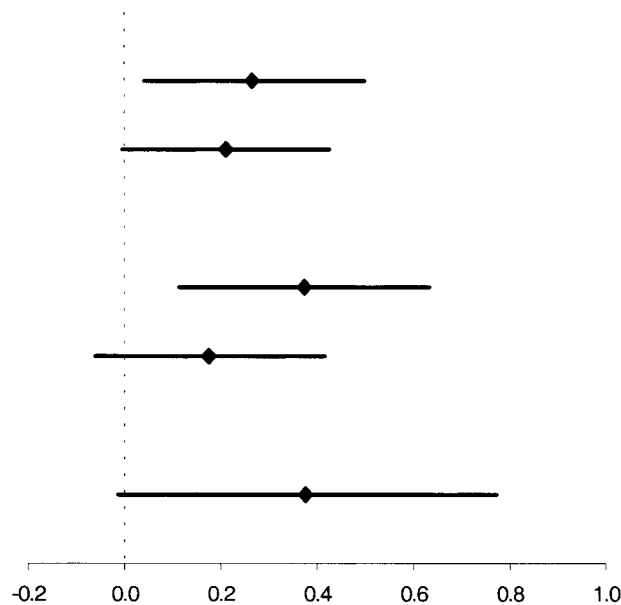


Fig 3. Independent predictors of worse primary AVF survival (P), including (early failure [EF] = 1) and excluding early failures (EF = 0) and secondary AVF survival (S). Hazard ratios (HR) expressed using a logarithmic scale.

Variables in the equations (hypothesis testing) with the associated HR (95%CI) and logHR (95%CI)

PRIMARY SURVIVAL (EF = 1)

Presence vs. absence of diabetes ($p=0.01$)
HR = 1.85 (1.1 to 3.16); logHR = 0.27 (0.04 to 0.5)

Catheter vs. AVF at initiation ($p=0.05$)
HR = 1.63 (0.99 to 2.67); logHR = 0.21 (-0.004 to 0.43)

PRIMARY SURVIVAL (EF = 0)

Presence vs. absence of diabetes ($p=0.005$)
HR = 2.37 (1.3 to 4.3); logHR = 0.37 (0.11 to 0.63)

Catheter vs. AVF at initiation ($p=0.14$)
HR = 1.5 (0.87 to 2.61); logHR = 0.18 (-0.06 to 0.42)

SECONDARY SURVIVAL

Presence vs. absence of diabetes ($p=0.04$)
HR = 2.38 (0.97 to 5.91); logHR = 0.38 (-0.01 to 0.77)

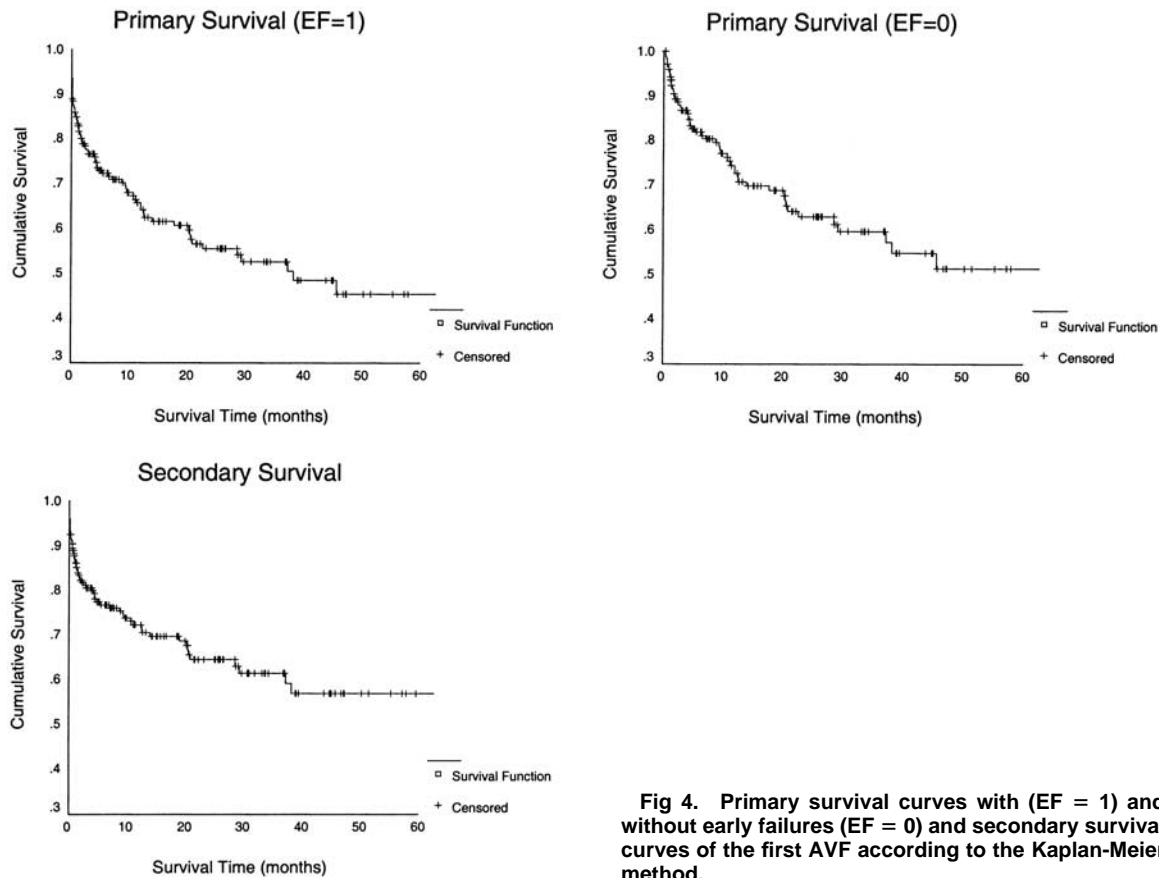


Fig 4. Primary survival curves with (EF = 1) and without early failures (EF = 0) and secondary survival curves of the first AVF according to the Kaplan-Meier method.

DISCUSSION

Results of this study confirm the high proportion of sick and elderly patients entering dialysis programs during the last decade.^{21,22} Furthermore, they highlight the negative impact on VA outcomes of late referral or poor predialysis follow-up, as well as the potential advantage of the direct involvement of nephrologists in the management of VA surgery.

Although less frequently diabetic than the American ESRD population, our patients were an average of 5 to 10 years older than those in other recently published series and had comorbid conditions similar to those in the United States and other industrialized countries.^{6,7,11,14} We nevertheless tried to give a native AVF to all patients: 81.2% of 197 consecutive patients had a distal AVF as their first VA. Those who received a proximal AVF were more likely to be older and women. This policy has led to a high proportion of native AVFs among prevalent HD patients in

our center, although preintervention vascular mapping was not routinely used.^{23,24}

The high prevalence of comorbidity and high proportion of patients older than 65 years in our cohort explain the relatively high mortality rates, which were significantly worse among patients with diabetes, as in other series.^{14,25} However, the cumulative 2-year survival rate of our patients (65%) is similar to the 67% reported in a recent analysis of European data relating to almost 60,000 patients who began renal replacement therapy during the last decade.²²

Our study confirms the low proportion of patients who begin HD therapy with an AVF in the absence of specific predialysis interventions. The absence of previous regular follow-up and, consequently, a nephrologist visit during the 2 to 6 months preceding dialysis are the strongest predictors of catheter use during the first HD therapy. It is worth noting that our patients with comorbid conditions and risk factors were re-

ferred late more frequently, as reported by other investigators.

Two recent large-scale studies^{4,26} observed 66% and 68% prevalences of catheter use in incident HD patients and showed the benefits of earlier referral; however, the use of AVFs in patients seen by a nephrologist well in advance of the need for chronic HD therapy was still suboptimal. We also found that moderate or severe comorbid conditions were associated with a lower likelihood for the use of an AVF at the start of HD therapy, thus confirming the need to refer such cases earlier. Furthermore, Dhingra et al,¹ analyzing a random sample of 5,507 prevalent HD patients from the US Renal Data System Mortality and Morbidity Study Wave 1, found that the risk for death from cardiovascular disease or infections was greater in patients both with and without diabetes with catheters and grafts than in those with AVFs. It recently was reported that in comparison to native AVFs, use of grafts or permanent or temporary catheters increased the risk for infection by more than twice, 13.6 and 32.6 times, respectively.²⁷ Moreover, as suggested by our findings, Q_B after 1 month and delivered dialysis dose at 3 months are significantly greater in patients with an AVF than those with a catheter. The presence of any comorbidity and absence of previous renal care significantly increased the chance of having a temporary access at the start of HD therapy, thus indicating that patients who receive less predialysis care and carry a heavier comorbidity burden also are more likely to start HD therapy with a catheter, with a greater risk for inadequate dialysis, morbidity, and mortality.²⁸

In comparison to the United States, a greater proportion of European patients see a nephrologist before starting HD therapy.¹¹ In our series, 37.1% of patients started HD therapy without previous renal care, and only 41.6% had seen a renal specialist at least 1 year before ESRD. Referral patterns and prevalent type of VA at the start of HD therapy in our area are more similar to those reported in America than in Europe.

The choice of grafts or permanent catheters as secondary VAs varies among countries. Pisoni et al¹¹ were the first to make a direct broad-based comparison of VA use and survival in Europe and the United States on the basis of data from the Dialysis Outcomes and Practice Patterns

Study (DOPPS) and found that European countries make greater median use of AVFs among both prevalent and incident HD patients, less use of catheters and grafts, and have a lower proportion of incident patients without a permanent VA. It has been reported that the prevalence of grafts in America may be as high as 60%⁴ or 67%,²⁶ which is particularly alarming if we consider the association between cardiovascular disease and inflammation and that infectious diseases per se represent the second cause of death in the ESRD population. Only 2% of our prevalent HD patients had a graft VA, which is much less than the 10% prevalence observed in Europe.¹¹ This may have been caused by the direct involvement in VA surgery of dedicated physicians focused on the care of patients with ESRD, and perhaps also a lack of incentives for grafts.²⁶

For organizational reasons, nephrologists in Italy have been responsible for the management of VA surgery since the early 1960s. Access insertion and care were not among the priorities of surgeons at that time; therefore, surgical training became a part of the educational program of most nephrological schools.²⁹ Conversely, the role of renal physicians in interventional radiology (an emerging area in the United States) is limited. Involvement of nephrologists in the management of VA surgery can shorten the interval between the need for VA insertion or the diagnosis of complications and intervention; however, there also are some important drawbacks to this policy, such as a reduction in efforts to implement surveillance to allow elective revisions and a low rate of referrals to interventional radiology. The impact of revision on VA survival is still an open question,^{30,31} but the VA revision rate in our patients was less than that reported by other investigators.¹⁴

This may have been caused by the limited use of VA mapping and flow monitoring, which probably increased the likelihood of missing early stenoses and losing the AVF. Measures of dialysis adequacy are late indicators of VA dysfunction, and the absence of more accurate methods of follow-up surveillance is a limitation that must be considered to improve the quality of a VA program.³²⁻³⁴ Additionally, the choice of the wrist, with the aim of reducing the risk for complications and preserving proximal vessels, limits revisions along the forearm for distal AVFs.

Table 6. Comparative Cumulative Secondary Patency Rates in Recent Series of Patients Excluding Graft Recipients After 1, 2, 3, and 5 Years by AVF Location When Specified

Reference	Year	Study Design	No. of Patients	Mean Age (y)	Diabetes Mellitus (%)	Female Sex (%)	No. of VAs	AVF Location	Follow-Up (y)			
									1	2	3	5
Leapman et al ³⁵	1996	R	144	50	34	27	150	L	56			30
Enzler et al ⁴¹	1996	R	414	44	11*	44	429	L	74		64	
Yasuhara et al ³¹	1997	R	287	56	28	36	287	All	94	92		89
Kalman et al ⁶	1999	P	384	59†	40	40	466	All		70		
Gibson et al ⁴²	2001	R	673	66	54	47	673	All		63		
Oliver et al ¹⁶	2001	R	115	56	45	41	115	U	64			
Bacchini et al ¹²	2001	R	404	65	18	42	462	All	72	68		50
Konner ¹⁴	2001	R	347	59	22	43	347	All	75‡	58‡	53‡	
Dixon et al ⁷	2002	P	73	52	45	18	73	L	54.8		47	37
			75	59	52	45	75	U	69.7		59.5	59.5
Pisoni et al ¹¹	2002	P										
<i>TC present (EU)</i>			164	60	22	43	164	All	65			
<i>TC present (US)</i>			209	60	46	47	209	All	53			
<i>TC absent (EU)</i>			430	60	22	43	430	All	83			
<i>TC absent (US)</i>			428	60	46	47	428	All	68			
Present series		P	197	66	22	40	197	All	72	64	62	

Abbreviations: R, retrospective; P, prospective; L, distal; U, proximal; TC, temporary catheter.

*Only diabetic glomerulosclerosis as the primary cause of nephropathy.

†Median value.

‡Only primary survival (primary patency rates) was reported.

This conservative policy can result in shorter secondary survival and explains our low revision rate.

In terms of VA survival, our results are similar to those of recent and less recent studies, with the latter surely involving less problematic patients. Cumulative secondary patency rates of the first AVF in comparison with other series are listed in Table 6.

Although there is a general consensus that older age, female sex, diabetes, neoplasm, cardiovascular disease, body size, and general health influence the quality of arteries and veins used to create an AVF,^{1,26} data concerning their impact on VA survival sometimes are conflicting. We found that only diabetes and previous use of a catheter had an impact on survival, although this nondefinitive result needs to be confirmed by larger epidemiological studies. Some investigators have shown a greater risk for failure in the presence of diabetes,^{6,15,35-37} but others have not.^{7,14,23,38}

Konner³⁹ recently reported his experience of increasing the proportion of patients with diabetes with native AVFs, stressing the importance of preserving the vascular bed in patients with ESRD and guaranteeing continuous surveillance by re-

nal staff to allow elective revisions.³⁹ His VA data showed similar primary survival in patients with and without diabetes, with a median time to the first event of 42.3 and 45.8 months, respectively. As a result of his policy to increase the number of proximal AVFs in patients with diabetes, the proportion of patients with diabetes with distal AVFs was only 25%, unlike in our series.¹⁴ Comparing these data with ours, we hypothesize that primary and secondary survival can be improved by optimizing preoperative investigations to select better arteries and veins and by AVF monitoring for timely triggered revisions, respectively. The trade-off of these strategies could be a greater complication rate because of a greater use of proximal sites, particularly in patients with diabetes.

Our findings do not confirm previous reports of worse results in patients previously treated with PD therapy,⁴⁰ possibly because of the short duration of PD therapy in our series because of early switching in the case of suboptimal intracorporeal treatment. Surgeon,^{7,36} hyperlipidemia,⁷ presence of neoplasm,^{1,26} female sex,^{11,16,37,38,41-43} distal rather than proximal location,⁷ peripheral vascular disease,^{5,11} and older age³⁵⁻³⁷ also have been described as risk factors for VA failure.

Some investigators recommend avoiding the wrist in elderly patients with diabetes.^{14,37,39} In our center, older age does not seem to affect AVF failure significantly and independently. It is interesting to note that the presence of a catheter at the beginning of HD therapy also was found to be a predictor of shorter survival in the DOPPS.¹¹ In our series, 1-year AVF patency rates in the presence (66%) or absence (80%) of catheters at the start of HD therapy were similar to those observed in European centers. Furthermore, as suggested by these investigators and our data, this greater risk for failure may be explained by the shorter maturation time because of catheter complications.

In conclusion, patients who started HD therapy in our center during the last 7 years had a high prevalence of comorbid conditions. Nevertheless, they all received an AVF, although the prevalent type of VA used at the start of HD therapy was a temporary catheter. Moreover, late referral, less intensive predialysis renal care, and presence of comorbid conditions not only reduced the chance of having an AVF at the start of HD therapy, but also were associated with a greater risk for AVF failure.

The direct involvement of nephrologists in the management of VA surgery, referral patterns, and predialysis follow-up seem to be more important and productive targets than simply trying to control traditional cardiovascular risk factors in improving the quality of care of patients with ESRD.

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