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Chapter 8

Hemodialysis catheters increase mortality as compared to arteriovenous accesses especially in elderly patients

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ABSTRACT

Background: Catheter use has been associated with an increased mortality risk in hemodialysis patients. However, differences in the all-cause and cause-specific mortality risk between catheter use and arteriovenous access use in young and elderly hemodialysis patients has not yet been investigated.

Methods: In this prospective cohort study of 1109 incident hemodialysis patients from 38 centers in the Netherlands, hazard ratios (HRs) with 95% confidence intervals (95% CIs) were calculated for 2-year all-cause, infection-related, and cardiovascular mortality in patients with a catheter as compared to patients with an arteriovenous access stratified for age (< 65 years and ≥ 65 years).

Results: Of the 1109 patients, 919 had an arteriovenous access and 190 had a catheter. The mortality rate was 76 per 1000 person-years in young patients with an arteriovenous access, 129 per 1000 person-years in young patients with a catheter, 222 per 1000 person-years in elderly patients with an arteriovenous access, and 427 per 1000 person-years in elderly patients with a catheter. The adjusted HR was 3.15 (95% CI 2.09-4.75) for elderly patients with a catheter as compared to young patients with an arteriovenous access. The adjusted HRs in elderly patients with a catheter as compared to elderly patients with an arteriovenous access were 1.54 (95% CI 1.13-2.12) for all-cause mortality, 1.60 (95% CI 0.62-4.19) for infection-related mortality, and 1.67 (95% CI 1.04-2.68) for cardiovascular mortality.

Conclusion: Especially elderly hemodialysis patients with a catheter have an increased all-cause, infection-related and cardiovascular mortality risk as compared to patients with an arteriovenous access.

INTRODUCTION

Dialysis patients require a vascular access for hemodialysis therapy. However, vascular access problems are responsible for 25% to 50% of hospitalizations in hemodialysis patients and are also associated with high costs.[1-6] While evidence from randomized-controlled trials is lacking, there is a broad consensus that arteriovenous accesses (fistula or graft) are superior to central venous catheters. Catheter use for hemodialysis has been associated with an increased risk for thrombosis,[7,8] short access survival,[8,9] and an increased risk for infections.[10-13] Therefore, the National Kidney Foundation Kidney Disease Outcome Quality Initiative (NKF K/DOQI) guidelines[14] and the European Best Practice Guidelines[15] recommend the use of arteriovenous accesses instead of catheters for vascular access in hemodialysis patients.

Despite this preference and recommendation for arteriovenous access use instead of catheters, limited studies have investigated the association between catheter use and mortality in elderly hemodialysis patients. Three studies from the United States have reported an increased mortality risk in elderly hemodialysis patients (elderly defined as age ≥ 65 years in two studies and aged ≥ 67 years in one study) ranging from a 1.3 to 2.1-fold increased risk for mortality in patients with a catheter as compared to patients with an arteriovenous access.[16-18] Moreover, information about differences in the association between catheter use and all-cause and cause-specific mortality in incident hemodialysis patients is limited and needs further exploration. This information is important, since the cause-specific and all-cause mortality risk could be different in elderly patients as compared to young patients, leading to age-specific treatment strategies.

Therefore, we investigated the association between catheter use versus arteriovenous access use and effect on all-cause and cause-specific (infection-related and cardiovascular) mortality risk in elderly hemodialysis patients as compared to young hemodialysis patients from a Dutch cohort of incident dialysis patients.

METHODS

Patients

The Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD) is a prospective multicenter cohort study in which incident adult end-stage renal disease patients from 38 dialysis centers in the Netherlands were included.[19] All patients gave informed consent and the study was approved by all local medical ethics committees. We followed patients at three months and six months after start of dialysis and thereafter every six months until death or censoring, i.e. transfer to a nonparticipating dialysis center, withdrawal from the study, transplantation, or end of the follow-up period (April 2006).

Eligibility included age older than 18 years, no previous renal replacement therapy, and survival of the initial three months of dialysis. For the current analyses, we used data from hemodialysis patients included between January 1997 and April 2004. The baseline was defined at three months after the start of dialysis. This time point of three months was chosen because patients' switch to another therapy or deaths within this period were most probably due to their health status before the start of dialysis, rather than to the dialysis modality.

Demographic and clinical data

Data on age, sex, primary kidney disease, comorbidity, predialysis care, diabetes, and cardiovascular disease (angina pectoris, myocardial infarction, heart failure, ischemic stroke, or claudication) were collected at the start of dialysis treatment. Primary kidney disease was classified according to the codes of the European Renal Association-European Dialysis and Transplant Association (ERA-EDTA).[20] We grouped patients into four classes of primary kidney disease: glomerulonephritis, diabetes mellitus, renal vascular disease, and other kidney diseases. Other kidney diseases consisted of patients with interstitial nephritis, polycystic kidney diseases, other multisystem diseases, and unknown diseases. The comorbidity was scored on the basis of the number comorbid conditions according to the comorbidity index described by Davies et al.[21]. The patients were classified as having no, intermediate, or severe comorbidity. Since comorbidity is an important confounder for the association between arteriovenous access use versus catheter use and mortality, the Davies score is used to adjust for comorbidity. The Davies score is based on the presence or absence of seven comorbid conditions, producing three risk groups. The Davies score assigns 1 point for each of the following conditions: ischemic heart disease (defined as prior myocardial infarction, angina pectoris, or ischemic changes on electrocardiogram), left ventricular dysfunction (defined as clinical evidence of pulmonary edema not due to errors in fluid balance), peripheral vascular disease (includes distal aortic, lower extremity, and cerebrovascular disease), malignancy, diabetes, collagen vascular disease, and other significant disorder (e.g. chronic obstructive pulmonary disease). Predialysis care was defined as a referral to a nephrologist for at least three months before initiation of dialysis to provide patients with adequate medical preparation.

Data on vascular access, Kt/Vurea delivered by hemodialysis, and body mass index (BMI) were collected at 3 months after the start of dialysis. Catheters included both tunneled and non-tunneled catheters (jugular and femoral) and arteriovenous accesses included native fistulas and grafts; data on native fistula and graft were not available, though. BMI was calculated as weight in kilograms divided by height in meters squared. The Kt/Vurea delivered by hemodialysis was estimated according to the second-generation Daugirdas formula on the basis of one plasma urea measurement before and one immediately after the dialysis session, the ultrafiltration, and the duration of the session as described previously.[22,23] Blood and 24-hour urine samples were obtained at 3 months after the start of dialysis. Albumin, creatinine, urea, cholesterol, and C-reactive protein (CRP) were determined from the blood samples. Urea and creatinine levels were also measured in the urine samples. Renal function, expressed as glomerular filtration rate (GFR), was calculated as the mean of creatinine and urea clearance corrected for body surface area (ml/min per 1.73 m^2). GFR was missing in 250 patients and serum albumin in 35 patients. The missing values for GFR and serum albumin were imputed with multiple imputation, a recommended technique where missing data for a subject are imputed by a value that is predicted by using the subject's other, known characteristics,[24,25] i.e. using demographic characteristics, mortality, catheter use and serum albumin, creatinine, and GFR at different time points. We used standard imputation methods in SPSS statistical software (version 17.0; SPSS, Chicago, Illinois).

Outcome definition

The endpoint of this study was 2-year mortality. We classified causes of death according to the codes of the ERA-EDTA and grouped death causes into cardiovascular, infection-related, and other mortality. The following codes were designated as cardiovascular mortality: myocardial ischemia and infarction; cardiac failure/fluid overload/pulmonary edema; cardiac arrest, cause unknown; cerebrovascular accident; hemorrhage from ruptured vascular aneurysm; mesenteric infarction; hyperkalemia; hypokalemia; cause of death uncertain/unknown. The following codes were designated as infection-related mortality: pulmonary infection; infections elsewhere except viral hepatitis; septicaemia; tuberculosis; generalized viral infection; peritonitis. All other deaths were designated as other.

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Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD) or as median and interquartile rage (IQR) depending on the normality of the data. Categorical variables are presented as number with valid percentages. For continuous data, differences for arteriovenous access use versus catheter use were tested with *t* test or Mann–Whitney–Wilcoxon test, depending on the distribution of the data. Chi-square test was used for categorical variables. A *P* value less than 0.05 was considered significant.

Survival curves were determined with the Kaplan-Meier method and mortality rates per 1000 person-years were calculated for four categories of hemodialysis patients defined by age group and vascular access (elderly arteriovenous access users aged ≥ 65 years, young arteriovenous access users aged < 65 years, elderly catheter users aged ≥ 65 years, and young catheter users aged < 65 years). We calculated crude and adjusted hazard ratios (HRs) with 95% confidence intervals (95% CIs) for all-cause, infection-related, and cardiovascular mortality within 2-year of follow-up in young and elderly hemodialysis patients using Cox proportional hazard analysis. Furthermore, we calculated HRs for elderly catheter users aged ≥ 65 years, elderly arteriovenous access users aged ≥ 65 years, and young catheter users aged < 65 years as compared to young arteriovenous access users aged < 65 years. In an additional analysis, HRs for mortality were calculated for very old patients with a catheter aged ≥ 75 years as compared to very old patients with an arteriovenous access and as compared to young patients with an arteriovenous access aged < 65 years. HRs were adjusted for age, sex, primary kidney disease, Davies comorbidity score, predialysis care, GFR, CRP, cholesterol, BMI, serum albumin levels, and Kt/Vurea delivered by hemodialysis. The association between catheter use and mortality was studied with an intention-to-treat design since we were interested in the effect of initial vascular access on mortality. All analysis have been done in SPSS statistical software version 17.0; SPSS, Chicago, Illinois.

RESULTS

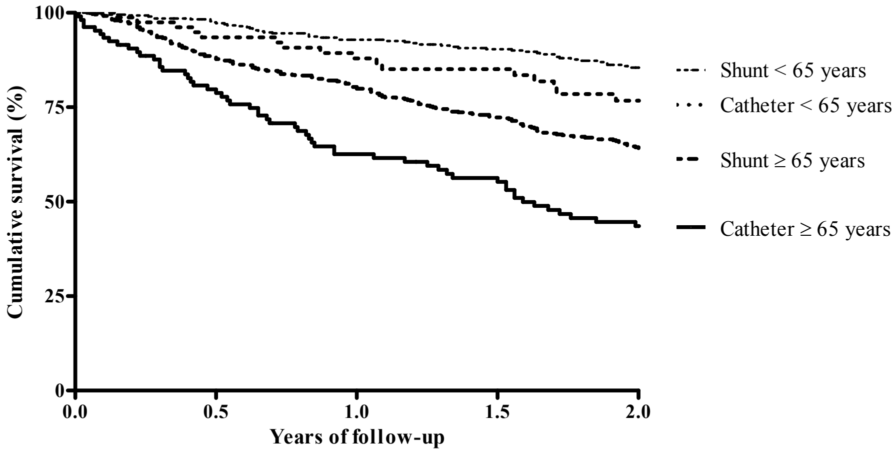
A total of 1109 patients were included between January 1997 and April 2004 and were treated with hemodialysis therapy at 3 months after start of dialysis in the NECOSAD. Of these patients, 190 (17.1%) had a catheter and 919 (82.9%) had an arteriovenous access for hemodialysis as vascular access. Table 1 shows the baseline characteristics of these patients. There were no differences between patients with a catheter or arteriovenous access according to age, sex, angina pectoris, myocardial infarction, ischemic stroke, claudication, diabetes, Davies comorbidity score, distribution of primary kidney disease, and Kt/Vurea delivered by hemodialysis. The patients with a catheter had a lower BMI, received less often predialysis care, had more often heart failure, had lower serum albumin levels, had lower cholesterol levels, had higher CRP levels, and had a lower GFR as compared to patients with an arteriovenous access ($p<0.05$ for all).

Table 1. Baseline characteristics

	Arteriovenous access N=919	Catheter N=190
Age (years) (%)	63.7 ± 13.6	63.2 ± 14.5
< 65 years	51.6 ± 10.6 (44.8)	50.1 ± 11.4 (44.2)
≥ 65 to 75 years	70.0 ± 2.9 (33.1)	70.1 ± 2.8 (33.2)
≥ 75 years	79.0 ± 3.1 (22.1)	78.8 ± 3.1 (22.6)
Sex, male (%)	58.7	55.8
BMI (kg/m^2)	24.7 ± 4.3	24.5± 4.5
Primary kidney disease (%)		
Diabetes mellitus	15.6	16.8
Glomerulonephritis	11.1	5.8
Renal vascular disease	21.0	27.4
Others	52.3	50.0
Cardiovascular disease (%)		
Angina pectoris	11.9	11.6
Myocardial infarction	13.5	15.3
Heart failure	12.1	20.5
Ischemic stroke	9.7	8.4
Claudication	16.2	17.9
Diabetes mellitus (%)	23.1	24.2
Davies comorbidity score (%)		
No	38.7	35.8
Intermediate	50.6	48.9
Severe	10.7	15.3
Predialysis care (%)	76.1	55.3
< 65 years	79.9	46.4
≥ 65 to 75 years	73.0	61.9
≥ 75 years	72.9	62.8
Serum albumin (g/L)	37.0 (33.3-40.0)	35.0 (32.0-38.0)
Cholesterol (mmol/L)	4.8 ± 1.2	4.5 ± 1.2
CRP (mg/L)	6.0 (3.0-12.5)	7.6 (3.0-13.0)
GFR (ml/min per 1.73 m^2)	3.1 (1.5-4.9)	2.9 (1.1-4.5)
Hemodialysis Kt/Vurea (week)	2.8 ± 0.8	2.8 ± 0.9

All-cause mortality

Of the 190 patients with a catheter, 72 patients died within two years. Of the 919 patients with an arteriovenous access, 217 died within two years. Figure 1 shows the Kaplan-Meier curves for all-cause mortality in young and elderly patients with an arteriovenous access or catheter for the first two years of follow-up. Table 2 shows the HRs for 2-year mortality for both age groups: young patients with a catheter as compared to young patients with an arteriovenous access and elderly patients with a catheter as compared to elderly patients with an arteriovenous access. The mortality rate was lowest for young arteriovenous access users and was highest for elderly catheter users. The HR for 2-year mortality was 1.54 (95% CI 0.87-2.74) in young patients with a catheter as compared to young patients with an arteriovenous access after adjustment for age, sex, primary kidney disease, Davies comorbidity score, angina pectoris, myocardial infarction, heart failure, ischemic stroke, claudication, predialysis care, GFR, CRP, cholesterol, BMI, serum albumin levels, and Kt/Vurea delivered by hemodialysis. The adjusted HR for 2-year mortality was 1.54 (95% CI 1.13-2.12) in elderly patients with a catheter as compared to elderly patients with an arteriovenous access. However, on an absolute scale catheter use in elderly patients as compared to arteriovenous access use in elderly is associated with more deaths than catheter use in young patients as compared to arteriovenous access use in young patients (absolute risk difference of 205 per 1000 person-years versus 53 per 1000 person-years). As compared to young patients with an arteriovenous access, both young patients with a catheter and elderly patients with a catheter or arteriovenous access had an increased risk (Table 3); elderly patients with a catheter had an almost 6-fold crude and 3-fold adjusted increased mortality risk as compared to young patients with an arteriovenous access.



Number at risk:

Shunt < 65 years	412	371	320	273	235
Catheter < 65 years	84	70	62	54	42
Shunt ≥ 65 years	507	424	376	325	282
Catheter ≥ 65 years	106	80	61	53	41

Figure 1. Kaplan-Meier survival curve for arteriovenous access versus catheter in young and elderly hemodialysis patients

Table 2. All-cause mortality for catheter as compared to arteriovenous access in young and elderly hemodialysis patients

		Arteriovenous access (graft or fistula)	Catheter
Young	Mortality rate per 1000 py	76	129
< 65 years	Crude HR (95% CI)	1 (reference)	1.70 (0.97-2.99)
	Adjusted* HR (95% CI)	1 (reference)	1.74 (0.99-3.08)
	Adjusted† HR (95% CI)	1 (reference)	1.54 (0.87-2.74)
Elderly	Mortality rate per 1000 py	222	427
≥ 65 years	Crude HR (95% CI)	1 (reference)	1.93 (95% CI 1.42-2.61)
	Adjusted* HR (95% CI)	1 (reference)	1.70 (95% CI 1.25-2.31)
	Adjusted† HR (95% CI)	1 (reference)	1.54 (95% CI 1.13-2.12)

py, person-years; HR, hazard ratio; CI, confidence interval. *Adjusted for age, sex, Davies comorbidity score, angina pectoris, myocardial infarction, heart failure, ischemic stroke, claudication, and primary kidney disease. †Additional adjusted for predialysis care, GFR, CRP, cholesterol, BMI, serum albumin levels, and hemodialysis Kt/Vurea.

Table 3. All-cause mortality for young and elderly patients with a catheter or arteriovenous access

	Mortality rate per 1000 person-years	Crude HR (95% CI)	Adjusted* HR (95% CI)	Adjusted† HR (95% CI)
Arteriovenous access < 65 years	76	1 (reference)	1 (reference)	1 (reference)
Catheter < 65 years	129	1.70 (0.97-2.99)	1.71 (0.97-3.02)	1.49 (0.84-2.66)
Arteriovenous access ≥ 65 years	222	2.93 (2.13-4.02)	2.12 (1.53-2.94)	2.06 (1.48-2.86)
Catheter ≥ 65 years	427	5.64 (3.84-8.27)	3.55 (2.39-5.28)	3.15 (2.09-4.75)

HR, hazard ratio; CI, confidence interval. *Adjusted for sex, Davies comorbidity score, angina pectoris, myocardial infarction, heart failure, ischemic stroke, claudication, and primary kidney disease. †Additional adjusted for predialysis care, GFR, CRP, cholesterol, BMI, serum albumin levels, and hemodialysis Kt/Vurea.

Cause-specific mortality

Of the 72 patients with a catheter who died within the first two years of follow-up, 7 died because of infections (1 young and 6 elderly patients), 34 because of cardiovascular causes (9 young and 25 elderly patients), and 31 died because of other reasons (6 young and 25 elderly patients). Of the 217 patients with an arteriovenous access who died within 2 years of follow-up, 27 died because of infections (7 young and 20 elderly patients), 103 because of cardiovascular causes (25 young and 78 elderly patients), and 87 died because of other reasons (17 young and 70 elderly patients). Figure 2 shows the adjusted HRs for cause-specific 2-year mortality in young and elderly patients. The adjusted HRs in elderly patients with a catheter were 1.60 (95% CI 0.62-4.19) for infection-related mortality and 1.67 (95% CI 1.04-2.68) for cardiovascular mortality as compared to elderly patients with an arteriovenous access. HRs in elderly patients with a catheter as compared to young patients with an arteriovenous access were 2.92 (95% CI 0.91-9.37) for infection-related mortality and 3.09 (95% CI 1.70-5.60) for cardiovascular mortality after adjustment for sex, primary kidney disease, Davies comorbidity score, angina pectoris, myocardial infarction, heart failure, ischemic stroke, claudication, predialysis care, GFR, CRP, cholesterol, BMI, serum albumin levels, and Kt/Vurea delivered by hemodialysis.

Very old patients

There were 43 very old (aged≥ 75 years) patients with a catheter, 26 patients of whom died within two years (11 cardiovascular causes, 3 infection-related causes, and 12 other causes). Furthermore, 72 patients of the 203 very old patients with an arteriovenous access died within two years (32 cardiovascular causes, 8 infection-related causes, and 32 other causes). The mortality rate per 1000 person-years was 244 for very old arteriovenous access users and 505 for very old catheter users. The adjusted HRs in very old patients were 1.83 (95% CI 1.14-2.93) for all-cause mortality, 2.32 (95% CI 0.57-9.40) for infection-related mortality, and 1.96 (95% CI 0.96-4.02) for cardiovascular mortality as compared to very old patients with an arteriovenous access.

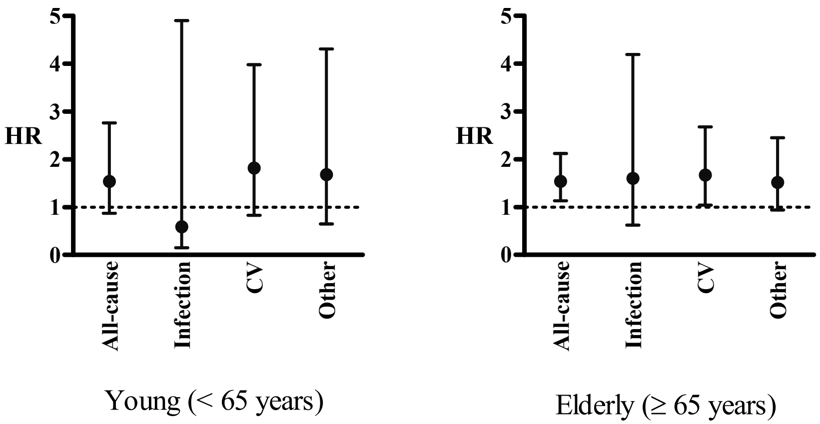


Figure 2. Adjusted hazard ratios with 95% confidence intervals for all-cause and cause-specific mortality for catheter as compared to arteriovenous access in young and elderly hemodialysis patients

Hazard ratios are adjusted for age, sex, Davies comorbidity score, angina pectoris, myocardial infarction, heart failure, ischemic stroke, claudication, primary kidney disease, predialysis care, GFR, CRP, cholesterol, BMI, serum albumin levels, and hemodialysis Kt/Vurea.

DISCUSSION

In this prospective cohort study of incident dialysis patients, we showed that catheter use was associated with an increased 2-year all-cause mortality risk as compared to arteriovenous access use. Elderly patients (aged ≥ 65 years) with a catheter had a 54% increased risk for mortality within 2 years as compared to elderly patients with an arteriovenous access and had a 3-fold increased risk for mortality within 2 years as compared to young patients (aged < 65 years) with an arteriovenous access. Very old patients with a catheter (aged ≥ 75 years) had an 83% increased mortality risk as compared to very old patients with an arteriovenous access. Among elderly patients, catheter use increased especially infection-related and cardiovascular mortality as compared to arteriovenous access use. The occurrence of septicemia or bacteremia has been shown to be associated with subsequent cardiovascular morbidity and mortality.[26] Our findings provide support to the guidelines which indicate that the use of catheters for hemodialysis should be discouraged. We showed that, especially in elderly hemodialysis patients, catheter use should be discouraged, since older age and catheter use are associated with an even higher increased mortality risk.

The 1.54-fold increased risk for mortality within two years of follow-up in elderly hemodialysis patients in our Dutch cohort is comparable to the increased risk found in cohorts from the United States. Three studies have reported a 1.3- to 2.1-fold increased risk for mortality in elderly patients with a catheter as compared to elderly patients with an arteriovenous access.[16-18] The first study used data from the United States Medicare dialysis population from 1995 to 1997.[16] They showed that catheter use was associated with a 1.7-fold increased one-year mortality as compared to native fistula use in elderly dialysis patients aged ≥ 67 years. The second study used data from the United States Renal Data System.[17] They showed in a subgroup analysis that catheter use was associated with a 2.1-fold increased mortality as compared to native fistula use in elderly dialysis patients aged ≥ 65 years over a mean follow-up of one year. Finally, the Choices for Healthy Outcomes in Caring for End-stage renal disease study showed in a subgroup analysis that catheter use was associated with a 1.3-fold increased mortality as compared to native fistula use in elderly dialysis patients aged ≥ 65 years over a follow-up of three years.[18]

Previous studies have reported that catheter use is associated with sepsis and bacteremia,[10-13] with decreased delivered dose of dialysis due to decreased blood flow rates,[27] and higher levels of inflammatory factors.[28] In addition, several studies have shown an increased infection-related and cardiovascular mortality risk in patients with a catheter as vascular access, especially in the first three months of dialysis.[29,30] However, to our knowledge, there are no studies that investigated infection-related or cardiovascular mortality associated with catheter use in elderly patients. We showed that elderly patients with a catheter had a 60% increased risk for infection-related mortality and a 67% increased risk for cardiovascular mortality as compared to elderly patients with an arteriovenous access. Including the first three months of dialysis would probably have led to an even higher infection-related mortality. Furthermore, we showed that very old patients with a catheter had a 2.3-fold increased risk for infection-related mortality and a 2.0-fold increased risk for cardiovascular mortality as compared to very old patients with an arteriovenous access. The confidence intervals for the HR for the infection-related 2-year mortality were wide due to a low number of patients with infection-related mortality.

Missing values for GFR and serum albumin were imputed. Patients with missing GFR or serum albumin used more often catheters and had relatively higher mortality rates. Analyses excluding patients who had a missing GFR or serum albumin values would have led to biased results, since relative more patients with a catheter with higher mortality rates would have been excluded.[24] This would have resulted in a decreased mortality risk for catheter use as compared to arteriovenous access use. Therefore, imputation of GFR and serum albumin using demographic characteristics, mortality, catheter use, and creatinine, serum albumin and GFR at different time points leads to more reliable results.

The comparison between catheter use and arteriovenous access use in an observational design makes confounding-by-indication the most important obstacle. It is important to realize that these observational studies have limitations to prove causality, since the observed increased mortality risk in patients with a catheter may partly reflect the effect of differences between arteriovenous access and catheter users. Catheter use has been associated with less predialysis care, lower GFR, lower serum albumin levels, and more co-morbidity as compared to arteriovenous access users.[31-33] In our analyses, we took this into account by correcting for these confounders, but this cannot exclude possible residual confounding. Therefore, our study shows that catheter use is associated with an increased mortality risk, but this does not necessarily prove that catheter use increases mortality risk. However, even additional adjustment for diabetes, angina pectoris, myocardial infarction, heart failure, ischemic stroke, and claudication did not change the results. Furthermore, we compared catheter use with arteriovenous access use and not with native fistula use since this information was lacking in our study. Therefore, as according to the literature mortality is higher in patients with a graft compared to patients with a native fistula,[18,30] patients with catheters in our study would have had even higher relative mortality risks. Moreover, we had no information about the type of catheters (tunneled or non-tunneled), the insertion place of the catheters, and the use of antimicrobial locks for catheters to investigate differences in mortality risk in patients with a catheter. An intention-to-treat analysis was chosen for the analyses, because we were interested in the association between mortality and initial vascular access treatment in elderly dialysis patients. This is important, since guidelines especially discourage catheter use as initial vascular access treatment.[14,15] In addition, an intention-to-treat analysis also avoids bias caused by transferring patients with an arteriovenous access with complications to the catheter group. An as-treated design would therefore overestimate the mortality-risk for patients with a catheter.

In conclusion, our study shows that catheter compared to arteriovenous access use is associated with an increased mortality, especially among elderly patients. Our findings are consistent with the guidelines which indicate that the use of catheters for hemodialysis should be discouraged. We showed that this is especially true for the elderly hemodialysis population.

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REFERENCES

1. Carlson DM, Duncan DA, Naessens JM, Johnson WJ. Hospitalization in dialysis patients. *Mayo Clin Proc*. 1984;59:769-775.
2. Fan PY, Schwab SJ. Vascular access: concepts for the 1990s. *J Am Soc Nephrol*. 1992;3:1-11.
3. Feldman HI, Held PJ, Hutchinson JT, Stoiber E, Hartigan MF, Berlin JA. Hemodialysis vascular access morbidity in the United States. *Kidney Int*. 1993;43:1091-1096.
4. Feldman HI, Kobrin S, Wasserstein A. Hemodialysis vascular access morbidity. *J Am Soc Nephrol*. 1996;7:523-535.
5. Ifudu O, Mayers JD, Cohen LS, Paul H, Brezsnyak WF, Avram MM, Herman AI, Friedman EA. Correlates of vascular access and nonvascular access-related hospitalizations in hemodialysis patients. *Am J Nephrol*. 1996;16:118-123.
6. Mayers JD, Markell MS, Cohen LS, Hong J, Lundin P, Friedman EA. Vascular access surgery for maintenance hemodialysis. Variables in hospital stay. *ASAIO J*. 1992;38:113-115.
7. Schwab SJ, Buller GL, McCann RL, Bollinger RR, Stickel DL. Prospective evaluation of a Dacron cuffed hemodialysis catheter for prolonged use. *Am J Kidney Dis*. 1988;11:166-169.
8. Suhocki PV, Conlon PJ, Jr., Knelson MH, Harland R, Schwab SJ. Silastic cuffed catheters for hemodialysis vascular access: thrombolytic and mechanical correction of malfunction. *Am J Kidney Dis*. 1996;28:379-386.
9. Schwab SJ. Assessing the adequacy of vascular access and its relationship to patient outcome. *Am J Kidney Dis*. 1994;24:316-320.
10. Taylor GD, McKenzie M, Buchanan-Chell M, Caballo L, Chui L, Kowalewska-Grochowska K. Central venous catheters as a source of hemodialysis-related bacteremia. *Infect Control Hosp Epidemiol*. 1998;19:643-646.
11. Kairaitis LK, Gottlieb T. Outcome and complications of temporary haemodialysis catheters. *Nephrol Dial Transplant*. 1999;14:1710-1714.
12. Powe NR, Jaar B, Furth SL, Hermann J, Briggs W. Septicemia in dialysis patients: incidence, risk factors, and prognosis. *Kidney Int*. 1999;55:1081-1090.
13. Oliver MJ, Rothwell DM, Fung K, Hux JE, Lok CE. Late creation of vascular access for hemodialysis and increased risk of sepsis. *J Am Soc Nephrol*. 2004;15:1936-1942.
14. Clinical practice guidelines for hemodialysis adequacy, update 2006. *Am J Kidney Dis*. 2006;48 Suppl 1:S2-90.
15. Tordoir J, Canaud B, Haage P, Konner K, Basci A, Fouque D, Kooman J, Martin-Malo A, Pedrini L, Pizzarelli F, Tattersall J, Vennegoor M, Wanner C, ter Wee P, Vanholder R. EBPG on Vascular Access. *Nephrol Dial Transplant*. 2007;22 Suppl 2:ii88-117.
16. Xue JL, Dahl D, Ebben JP, Collins AJ. The association of initial hemodialysis access type with mortality outcomes in elderly Medicare ESRD patients. *Am J Kidney Dis*. 2003;42:1013-1019.
17. Foley RN, Chen SC, Collins AJ. Hemodialysis access at initiation in the United States, 2005 to 2007: still “catheter first”. *Hemodial Int*. 2009;13:533-542.
18. Astor BC, Eustace JA, Powe NR, Klag MJ, Fink NE, Coresh J. Type of vascular access and survival among incident hemodialysis patients: the Choices for Healthy Outcomes in Caring for ESRD (CHOICE) Study. *J Am Soc Nephrol*. 2005;16:1449-1455.
19. Drechsler C, Grootendorst DC, Boeschoten EW, Krediet RT, Wanner C, Dekker FW. Changes in parathyroid hormone, body mass index and the association with mortality in dialysis patients. *Nephrol Dial Transplant*. 2010.

20. van Dijk PC, Jager KJ, de Charro F, Collart F, Cornet R, Dekker FW, Gronhagen-Riska C, Kramar R, Leivestad T, Simpson K, Briggs JD. Renal replacement therapy in Europe: the results of a collaborative effort by the ERA-EDTA registry and six national or regional registries. *Nephrol Dial Transplant*. 2001;16:1120-1129.

21. Davies SJ, Russell L, Bryan J, Phillips L, Russell GI. Comorbidity, urea kinetics, and appetite in continuous ambulatory peritoneal dialysis patients: their interrelationship and prediction of survival. *Am J Kidney Dis*. 1995;26:353-361.

22. Daugirdas JT. Second generation logarithmic estimates of single-pool variable volume Kt/V: an analysis of error. *J Am Soc Nephrol*. 1993;4:1205-1213.

23. Termorshuizen F, Dekker FW, van Manen JG, Korevaar JC, Boeschoten EW, Krediet RT. Relative contribution of residual renal function and different measures of adequacy to survival in hemodialysis patients: an analysis of the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD)-2. *J Am Soc Nephrol*. 2004;15:1061-1070.

24. Donders AR, van der Heijden GJ, Stijnen T, Moons KG. Review: a gentle introduction to imputation of missing values. *J Clin Epidemiol*. 2006;59:1087-1091.

25. van Buuren S, Boshuizen HC, Knook DL. Multiple imputation of missing blood pressure covariates in survival analysis. *Stat Med*. 1999;18:681-694.

26. Ishani A, Collins AJ, Herzog CA, Foley RN. Septicemia, access and cardiovascular disease in dialysis patients: the USRDS Wave 2 study. *Kidney Int*. 2005;68:311-318.

27. Cortez AJ, Paulson WD, Schwab SJ. Vascular access as a determinant of adequacy of dialysis. *Semin Nephrol*. 2005;25:96-101.

28. Movilli E, Brunori G, Camerini C, Vizzardi V, Gaggia P, Cassamali S, Scolari F, Parrinello G, Cancarini GC. The kind of vascular access influences the baseline inflammatory status and epoetin response in chronic hemodialysis patients. *Blood Purif*. 2006;24:387-393.

29. Pastan S, Soucie JM, McClellan WM. Vascular access and increased risk of death among hemodialysis patients. *Kidney Int*. 2002;62:620-626.

30. Dhingra RK, Young EW, Hulbert-Shearon TE, Leavey SF, Port FK. Type of vascular access and mortality in U.S. hemodialysis patients. *Kidney Int*. 2001;60:1443-1451.

31. Stehman-Breen CO, Sherrard DJ, Gillen D, Caps M. Determinants of type and timing of initial permanent hemodialysis vascular access. *Kidney Int*. 2000;57:639-645.

32. Wasse H, Speckman RA, Frankenfield DL, Rocco MV, McClellan WM. Predictors of delayed transition from central venous catheter use to permanent vascular access among ESRD patients. *Am J Kidney Dis*. 2007;49:276-283.

33. Avorn J, Winkelmayer WC, Bohn RL, Levin R, Glynn RJ, Levy E, Owen W, Jr. Delayed nephrologist referral and inadequate vascular access in patients with advanced chronic kidney failure. *J Clin Epidemiol*. 2002;55:711-716.