Haemodialysis 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 haemodialysis patients. However, differences in the all-cause and cause-specific mortality risk between catheter use and arteriovenous access use in young and elderly haemodialysis patients have not yet been investigated.

Methods. In this prospective cohort study of 1109 incident haemodialysis patients from 38 centres 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.

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

Keywords: catheter; haemodialysis; mortality

Introduction

Dialysis patients require a vascular access for haemodialysis therapy. However, vascular access problems are responsible for 25–50% of hospitalizations in haemodialysis 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 haemodialysis has been associated with increased risk for thrombosis [7, 8], short access survival [8, 9] and increased risk for infections [10–13]. Therefore, the National Kidney Foundation Kidney Disease Outcome Quality Initiative guidelines [14] and the European Best Practice Guidelines [15] recommend the use of arteriovenous accesses instead of catheters for vascular access in haemodialysis 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 haemodialysis patients. Three studies from the USA have reported an increased mortality risk in elderly haemodialysis 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 haemodialysis patients is limited and needs further exploration. This information is important since the cause-specific and/or 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 haemodialysis patients as...
compared to young haemodialysis patients from a Dutch cohort of incident dialysis patients [19].

Materials and methods

Patients

The Netherlands Cooperative Study on the Adequacy of Dialysis (NECOD-SAD) is a prospective multicentre cohort study in which incident adult end-stage renal disease patients from 38 dialysis centres 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 3 and 6 months after start of dialysis and thereafter every 6 months until death or censoring, i.e. transfer to a non-participating dialysis centre, withdrawal from the study, transplantation or end of the follow-up period (April 2006).

Eligibility included age >18 years, no previous renal replacement therapy and survival of the initial 3 months of dialysis. For the current analyses, we used data from haemodialysis patients included between January 1997 and April 2004. The baseline was defined at 3 months after the start of dialysis. This time point of 3 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, pre-dialysis care, diabetes and cardiovascular disease (angina pectoris, myocardial infarction, heart failure, ischaemic 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: ischaemic heart disease (defined as prior myocardial infarction, angina pectoris or ischaemic changes on electrocardiogram), left ventricular dysfunction (defined as clinical evidence of pulmonary oedema 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). Pre-dialysis care was defined as a referral to a nephrologist for at least 3 months before initiation of dialysis to provide patients with adequate medical preparation.

Data on vascular access, Kt/Vurea delivered (Kt/Vurea) by haemodialysis and body mass index (BMI) were collected at 3 months after the start of dialysis. Catheters included both tunnelled and non-tunnelled 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 by haemodialysis 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-h urine samples were obtained at 3 months after the start of dialysis. Albumin, creatinine, urea, cholesterol and C-reactive protein (CRP) were determined in blood samples. Urea and creatinine levels were also measured in 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 m²). 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, IL).

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 ischaemia and infarction; cardiac failure/ fluid overload/ pulmonary oedema; cardiac arrest, cause unknown; cerebrovascular accident; haemorrhage from ruptured vascular aneurysm; mesenteric infarction; hyperkalaemia; hypokalaemia and cause of death uncertain/unknown. The following codes were designated as infection-related mortality: pulmonary infection, infections elsewhere except viral hepatitis, septicemia, tuberculosis, generalized viral infection and peritonitis. All other deaths were designated as other.

Statistical analysis

Continuous variables are presented as mean ± SD or as median and interquartile range 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 < 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 haemodialysis 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 years of follow-up in young and elderly haemodialysis 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, pre-dialysis care, GFR, CRP, cholesterol, BMI, serum albumin levels and Kt/Vurea delivered by haemodialysis. 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 analyses have been done in SPSS statistical software version 17.0 (SPSS).

Results

A total of 1109 patients were included between January 1997 and April 2004 and were treated with haemodialysis 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 haemodialysis 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, ischaemic stroke, claudication, diabetes, Davies comorbidity score, distribution of primary kidney disease and Kt/Vurea delivered by haemodialysis. The patients with a catheter had a lower BMI, received less often pre-dialysis 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).
All-cause mortality

Of the 190 patients with a catheter, 72 patients died within 2 years. Of the 919 patients with an arteriovenous access, 217 died within 2 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 2 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, ischaemic stroke, claudication, pre-dialysis care, GFR, CRP, cholesterol, BMI, serum albumin levels and Kt/Vurea delivered by haemodialysis. 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 patients is associated with more deaths than that 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.

**Cause-specific mortality**

Of the 72 patients with a catheter, who died within the first 2 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 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 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 2.44 for very old arteriovenous access users and 505 for very old catheter users. The adjusted HRs in very old patients with a catheter 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 8.71 (95% CI: 1.04–2.68) for cardiovascular mortality as compared to very old patients with an arteriovenous access.

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

<table>
<thead>
<tr>
<th>Arteriovenous Access</th>
<th>Mortality rate per 1000 person-years</th>
<th>Crude HR (95% CI)</th>
<th>Adjusted HR (95% CI)</th>
<th>Adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catheter &lt;65 years</td>
<td>76</td>
<td>1 (reference)</td>
<td>1 (reference)</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>Elderly ≥65 years</td>
<td>222</td>
<td>2.93 (2.13–4.02)</td>
<td>3.55 (2.39–5.28)</td>
<td>3.15 (2.09–4.75)</td>
</tr>
</tbody>
</table>

**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...
Previous studies have reported that catheter use is associated with sepsis and bacteraemia [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 3 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 3 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 CIs 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 relatively 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 pre-dialysis care, lower GFR, lower serum albumin levels and more comorbidity 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, ischaemic 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

![Graph showing adjusted HRs with 95% CIs for all-cause and cause-specific mortality for catheter use compared to arteriovenous access in young and elderly haemodialysis patients. HRs are adjusted for age, sex, Davies comorbidity score, angina pectoris, myocardial infarction, heart failure, ischaemic stroke, claudication, primary kidney disease, pre-dialysis care, GFR, CRP, cholesterol, BMI, serum albumin levels and haemodialysis Kt/Vurea.](image-url)
had no information about the type of catheters (tunnelled or non-tunnelled), 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 haemodialysis should be discouraged. We showed that this is especially true for the elderly haemodialysis population.

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Conflict of interest statement. None declared.

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