



## Morbidity, mortality and quality of life in the ageing haemodialysis population: results from the ELDERLY study

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### Abstract

**Background:** The physical–functional and social–emotional health as well as survival of the elderly ( $\geq 75$  years of age) haemodialysis patient is commonly thought to be poor. In a prospective, multicentre, non-interventional, observational study, the morbidity, mortality and quality of life (QoL) in this patient group were examined and compared with a younger cohort.

**Methods:** In 92 German dialysis centres, 2507 prevalent patients 19–98 years of age on haemodialysis for a median of 19.2 months were included in a drug monitoring study of darbepoetin alfa. To examine outcome and QoL parameters, 24 months of follow-up data in the age cohorts  $< 75$  and  $\geq 75$  years were analysed. Treatment parameters, adverse and intercurrent events, hospitalizations, morbidity and mortality were assessed. QoL was evaluated by means of the 47-item Functional Assessment of Chronic Illness Therapy–Anaemia score (FACT-An, version 4).

**Results:** The 2-year mortality rate was 34.7% for the older cohort and 15.8% for the younger cohort. The mortality rate for the haemodialysed elderly patients was 6.2% higher in absolute value compared with the age-matched background population. A powerful predictor of survival was the baseline FACT-An score and a close correlation with the 20-item anaemia subscale (AnS) was demonstrated. While the social QoL in the elderly patients was more stable than in the younger cohort (leading to equivalent values at the end of the study period), a pronounced deterioration of physical and functional status was observed.

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The median number of all-cause hospital days per patient-year was 12.3 for the elderly cohort and 8.9 for the younger patient population. The overall 24-month hospitalization rate was only marginally higher in the elderly cohort (34.0 versus 33.3%).

**Conclusions:** In this observational study, the mortality rate of elderly haemodialysis patients was not exceedingly high compared with the age-matched background population. Furthermore, the hospitalization rate was only slightly higher compared with the younger age group and the median yearly hospitalization time trended lower compared with registry data. The social well-being of elderly haemodialysis patients showed a less pronounced decline over time and was equal to the score of the younger cohort at the end of the study period. The physical and functional status in the elderly patients was lower and showed a sharper decline over time. The baseline FACT-An score correlated closely with the 24-month survival probability.

**Key words:** chronic haemodialysis, elderly, quality of life, survival analysis, vascular access

## Introduction

The dialysis population is growing and ageing. All major renal registries have reported a steady increase in the proportion of elderly patients ( $\geq 75$  years old) requiring renal replacement therapy (RRT) [1–4]. According to records from the United States Renal Data System (USRDS), the adjusted incident rate of end-stage renal disease (ESRD) has grown  $\sim 12\%$  for patients  $\geq 75$  years of age since the year 2000. The average age of incident ESRD patients was 63 years in the 2009 cohort and 25% of patients were  $\geq 75$  years of age (mean age 82 years) [1]. Despite the high rate of cause-specific mortality in elderly patients with chronic kidney disease, a significant percentage progress to ESRD, underlining the importance of adequate nephrological care [5, 6]. Relatively poor functional status and outcomes have been reported for elderly haemodialysis patients, especially in negatively selected cohorts [7, 8]. USRDS statistics reveal that the expected remaining lifetime of an individual  $\geq 75$  years of age on RRT is  $\leq 3.1$  years but  $\leq 8.8$  years for the background population. Similar results are reported from the European Renal Association–European Dialysis and Transplant Association (ERA-EDTA) registry ( $\leq 3.4$  versus  $\leq 11.3$  years). According to USRDS data, the adjusted 2-year and 5-year survival rates for incident ESRD patients are as low as 41 and 13% (51 and 19% for ERA-EDTA data), respectively [1, 2]. The predominant treatment modality for incident and prevalent elderly ESRD patients is in-centre haemodialysis, while other modalities are reported with  $< 5\%$  for incident and  $< 12\%$  for prevalent patients [1]. To date there are only limited data on the determinants of survival, the degree of physical–functional fitness and social–emotional well-being of elderly haemodialysis patients, and there have been intense discussions about whether the expensive and resource-consuming procedure of haemodialysis is justified by acceptable outcomes and quality of life (QoL) in the elderly.

## Materials and methods

### Study design

In a prospective, longitudinal, nationwide, non-randomized study of haemodialysis patients receiving darbepoetin alfa (92 dialysis centres in different regions of Germany), QoL and treatment parameters, adverse and intercurrent events, hospitalizations, morbidity and mortality were assessed in the age groups  $\geq 75$  and  $< 75$  years. The patients were followed up for a period of 24 months. The ELDERLY project was sponsored by Amgen and was approved by national authorities. All included patients provided written, informed consent. The study was conducted in compliance with local ethical guidelines and the Declaration of Helsinki. All data were evaluated by an independent biostatistician.

### Study patients, data collection and definitions

Non-critically ill patients receiving in-centre haemodialysis for  $> 3$  months along with concomitant darbepoetin alfa therapy for the treatment of anaemia were eligible for the study. Baseline characteristics (see Table 1) were assessed at the time of enrolment and patients were then prospectively monitored using an observational plan. Adverse events and changes of darbepoetin alfa dose were continuously monitored. Dialysis parameters,

**Table 1.** Baseline demographic data<sup>a</sup>

	Age $< 75$ years	Age $\geq 75$ years
Age (years)		
Mean $\pm$ SD	62.5 $\pm$ 10.6	80.2 $\pm$ 3.9
95% CI for the mean	62.0–63.0	79.9–80.4
Sex, n (%)		
Male	1003 (58.6)	374 (47.0)
Female	708 (41.4)	422 (53.0)
BMI (kg/m <sup>2</sup> )		
Mean $\pm$ SD	26.4 $\pm$ 5.3	25.5 $\pm$ 4.7
95% CI for the mean	26.2–26.7	25.2–25.8
Dialysis vintage (months)		
Median	20.9	15.9
95% CI for the median	18.9–23.7	14.0–18.7
Vascular access, %		
Arteriovenous fistula	86.4	81.2
Arteriovenous graft	11.4	14.7
Catheter	2.2	4.1
Underlying disease, %		
Diabetic nephropathy	31.6	32.7
Chronic glomerular nephritis	20.7	12.3
Vascular nephropathy	13.6	28.1
Interstitial nephritis	8.6	7.8
Congenital nephropathy	6.4	1.9
Other renal disease	1.6	1.4
Unknown aetiology	17.5	15.8
Concomitant diseases, %		
Hypertension	87.4	80.7
Diabetes	41.9	46.6
Chronic heart disease	40.5	55.3
Peripheral arterial disease	23.7	29.5
Retinopathy	20.7	20.1
Polyneuropathy	18.6	21.5
Cerebrovascular insufficiency	13.5	23.5
Pulmonary disease	8.5	7.3
Malignancy	7.4	9.2
Amputation	6.3	4.5

<sup>a</sup>Assuming proportionally distributed events in missing cases when calculating percentages.

**Table 2.** Type of baseline treatment parameters and dialysis-associated complications during the observation period<sup>a</sup>

	Age <75 years	Age ≥75 years
Median dialysis dose (h/week)	12.0	12.0
Frequency of dialysis, %		
2× per week	4.4	7.2
3× per week	93.5	91.3
4× per week	1.3	1.5
Other	0.8	–
Median blood flow (mL/min)	280	250
Median ultrafiltration rate (mL/h)	600	500
Patients with dialysis-associated complications, %	53.8	60.4
Type of complication, %		
Muscle cramps	25.2	30.3
Hypotension	21.9	31.5
Hypertension	19.5	16.6
Itching	12.0	11.8
Polyneuropathic pain	10.8	11.4
Pain in bones or joints	9.6	12.2
Skin alterations	5.9	8.4
Allergic reactions	1.9	1.5
Carpal tunnel syndrome	1.3	1.9
Others	4.6	4.1

<sup>a</sup>Assuming proportionally distributed events in missing cases when calculating percentages.

**Table 3.** Comorbidity, hospitalization and survival

	Age <75 years	Age ≥75 years
Baseline Charlson comorbidity index, %		
2–4	36.2	–
5–6	38.9	40.3
≥7	24.9	59.7
Patients with hospitalization(s) in 24 months, %	33.3	34.0
Median hospital days per year	8.9	12.3
Survival (Kaplan–Meier estimators)		
Month 12	0.916	0.808
Month 24	0.829	0.628
Survival (Kaplan–Meier estimators)		
Public centres		
Month 12	0.968	0.915
Month 24*	0.899	0.765
Private centres		
Month 12	0.967	0.930
Month 24*	0.910	0.753
*Comparison of strata (log-rank test)	P = 0.39	P = 0.94
Yearly mortality rate, %	Elderly	DZA <sup>a</sup> 2006
<50 years	2.00	0.10
50–59 years	4.80	0.52
60–69 years	8.78	1.16
70–79 years	13.1	3.12
≥80 years	19.0	13.6

<sup>a</sup>German Centre of Gerontology (DZA: Deutsches Zentrum fuer Altersfragen).

dialysis-associated complications (see Table 2) and haemoglobin (Hb) levels were assessed monthly. The following data were collected every 3 months: dialysis adequacy, routine haematological and serum biochemical parameters, hospitalizations and comorbidities (see Tables 3 and 4). The comedication and number of transfusions were documented every 6 months. To describe and compare morbidity, the age-adjusted (1 point for each decade over the age of 40 years) Charlson comorbidity index (CCI) was used, with higher scores indicating greater comorbidity [11]. A strong correlation between the age-adjusted CCI score and mortality in maintenance RRT patients has been demonstrated [12]. The minimum score of all patients was 2 due to terminal renal failure. The minimum value in the elderly cohort was 6 as a result of the age adjustment. Furthermore, QoL parameters were evaluated at baseline and at 12 and 24 months in a sub-cohort of 68 participating centres (74%) by means of the Functional Assessment of Chronic Illness Therapy (FACIT) Anaemia score (FACT-An, version 4; see [www.facit.org](http://www.facit.org) for details) (n = 1373) [13]. Questions Results were measured on a 5-point scale (0–4 points). The total score was obtained by summing the four subscale scores for physical (PWB), social/family (SWB), emotional (EWB) and functional (FWB) well-being (equivalent to the FACT-General; 27 items) and adding the score for the anaemia subscale (AnS; 20 items). Score ranges were 0–24 (EWB; 6 items), 0–28 (PWB, SWB and FWB; 7 items each) and 0–80 (AnS), with higher scores indicating a better rehabilitation (total of 47 questions; maximum FACT-An score 188). On negatively phrased questions scores were reversed, and in case of skipped questions, the value was prorated using the score average in the individual subscale. The Trial Outcome Index (TOI) as an index of physical and functional outcome was determined by summing the PWB, FWB and AnS subscales. Assessment was performed by means of a paper case report form on a voluntary basis (24 centres opted out). In addition to QoL parameters, the

need for general nursing care was assessed at baseline. This is a technical term of disability in the German health care system to evaluate nursing staff requirements for inpatient care. Patients in levels A1–A3 are in need of basic support (personal hygiene, nutrition, mobility) for an average of ~1, 2 or 3 h/day, respectively. Depending on the amount of additional special care needed (e.g. infusions, wound dressings, assistance with medication intake), the calculated range of nursing staff required is 52–88 (A1), 98–134 (A2) and 178–215 (A3), respectively. For the sample size calculation, a 20% difference of target variables was regarded as clinically relevant and should be detectable (even in subgroups) with a precision <20% [length of 95% confidence interval (CI)]. Assuming a dropout rate of 20%, this leads to a total population size of 2500 patients (with at least one documented visit).

**Data management and statistical analyses**

Data tracking was performed using log files that were read into a global database using a validated check routine. In case of inconsistencies, a query was sent to the responsible clinical site. Outliers outside of the 4 σ region of the mean were eliminated in case the query was left unanswered. Statistical analyses were performed as an explorative evaluation with descriptive interpretation of differences between the subgroups. Calculations were performed within the SAS software version 9.1 (SAS Institute, Cary, NC, USA) on a Microsoft Windows operating system (Microsoft, Unterschleissheim, Germany). Where applicable, subgroup analyses were supplemented by multivariate procedures (logistic regression, Cox regression) to identify relevant predictors of the target variables and to study the influence of cofactors. Hazard ratios (HRs) were used to describe the results of the Cox analysis.

Table 4. Treatment quality (mean values), comedication<sup>a</sup> and QoL parameters (maximum likelihood estimates)

	Month	Age <75 years	Age ≥75 years
eKt/V <sup>b</sup>	0	1.32	1.29
	12	1.37	1.33
	24	1.46	1.40
	Change from BL <sup>c</sup>	<b>P &lt; 0.01</b>	<b>P &lt; 0.01</b>
Haemoglobin (g/dL)	0	11.6	11.8
	12	11.9	11.8
	24	11.8	11.8
	Change from BL	<b>P &lt; 0.01</b>	P = 0.94
Corrected total calcium (mmol/L)	0	2.30	2.31
	12	2.28	2.30
	24	2.26	2.28
	Change from BL	<b>P &lt; 0.01</b>	<b>P &lt; 0.01</b>
Phosphate (mmol/L)	0	1.90	1.72
	12	1.86	1.72
	24	1.81	1.72
	Change from BL	<b>P &lt; 0.01</b>	P = 1.00
Corrected calcium × phosphate product (mmol <sup>2</sup> /L <sup>2</sup> )	0	4.41	4.02
	12	4.23	3.98
	24	4.13	3.93
	Change from BL	<b>P &lt; 0.01</b>	P = 0.12
iPTH (pmol/L)	0	14.7	13.3
	12	16.1	14.2
	24	17.1	17.1
	Change from BL	<b>P &lt; 0.01</b>	<b>P &lt; 0.01</b>
Albumin (g/L)	0	40.1	38.7
	12	40.5	39.1
	24	40.6	38.9
	Change from BL	<b>P = 0.01</b>	P = 0.50
HbA1c (%)	0	6.16	6.07
	12	6.09	5.94
	24	6.03	5.96
	Change from BL	<b>P &lt; 0.01</b>	<b>P &lt; 0.05</b>
Transferrin saturation (%)	0	23.9	23.8
	12	25.7	24.5
	24	24.7	24.4
	Change from BL	<b>P &lt; 0.05</b>	P = 0.36
Ferritin (µg/L)	0	340	354
	12	476	485
	24	501	508
	Change from BL	<b>P &lt; 0.01</b>	<b>P &lt; 0.01</b>
CRP (mg/L)	0	6.12	6.82
	12	5.95	6.49
	24	6.02	6.79
	Change from BL	P = 0.66	P = 0.96
BMI (kg/m <sup>2</sup> )	0	26.4	25.6
	12	26.3	25.2
	24	26.1	25.0
	Change from BL	<b>P &lt; 0.01</b>	<b>P &lt; 0.01</b>
Weekly darbepoetin alfa dose (µg/week)	0	35.3	34.0
	12	32.1	31.5
	24	32.0	30.6
	Change from BL	<b>P &lt; 0.01</b>	<b>P &lt; 0.01</b>
Antihypertensive agents (excluding diuretics)	0	87.3%	84.4%
	12	84.6%	82.7%
	24	83.6%	81.6%
	Change from BL	<b>P &lt; 0.01</b>	<b>P &lt; 0.01</b>
Diuretics	0	69.3%	74.0%
	12	63.1%	68.8%
	24	59.0%	63.7%
	Change from BL	<b>P &lt; 0.01</b>	<b>P &lt; 0.01</b>
Cardiac glycosides	0	8.6%	14.1%
	12	9.3%	13.2%
	24	10.6%	13.5%
	Change from BL	<b>P &lt; 0.01</b>	<b>P &lt; 0.01</b>
Iron therapy	0	77.0%	79.3%
	12	69.2%	70.9%
	24	69.5%	70.8%
	Change from BL	<b>P &lt; 0.01</b>	<b>P &lt; 0.01</b>

Table continues

Table 4. Continued

	Month	Age <75 years	Age ≥75 years
Phosphate binders	0	81.9%	69.1%
	12	82.0%	73.3%
	24	82.4%	73.6%
Vitamin D	0	62.6%	60.1%
	12	62.6%	63.7%
	24	63.5%	69.5%
Physical well-being (PWB) (score range 0–28)	0	20.4	18.7
	12	20.2	18.2
	24	19.6	17.3
	Change from BL	–3.9%	–7.5%
		<b>P &lt; 0.01</b>	<b>P &lt; 0.01</b>
Social well-being (SWB) (score range 0–28)	0	21.0	20.8
	12	20.8	20.5
	24	20.4	20.4
	Change from BL	–2.9%	–1.9%
		<b>P &lt; 0.01</b>	<b>P = 0.37</b>
Emotional well-being (EWB) (score range 0–24)	0	17.1	16.4
	12	17.2	16.2
	24	16.9	15.8
	Change from BL	–1.2%	–3.7%
		<b>P = 0.23</b>	<b>P = 0.11</b>
Functional well-being (FWB) (score range 0–28)	0	16.0	14.5
	12	15.9	14.0
	24	15.4	12.6
	Change from BL	–3.8%	–13.1%
		<b>P &lt; 0.01</b>	<b>P &lt; 0.01</b>
FACT-G (score range 0–108) (PWB + SWB + EWB + FWB)	0	74.4	70.3
	12	73.9	68.7
	24	72.0	65.9
	Change from BL	–3.2%	–6.3%
		<b>P &lt; 0.01</b>	<b>P &lt; 0.01</b>
Anaemia subscale (AnS) (score range 0–80)	0	35.5	30.9
	12	35.0	30.5
	24	34.3	29.3
	Change from BL	–3.4%	–5.2%
		<b>P &lt; 0.01</b>	<b>P &lt; 0.05</b>
Trial Outcome Index (TOI) (score range 0–136) (PWB + FWB + AnS)	0	71.9	63.9
	12	71.0	62.5
	24	69.3	59.1
	Change from BL	–3.6%	–7.5%
		<b>P &lt; 0.01</b>	<b>P &lt; 0.01</b>
FACT-An (score range 0–188) (FACT-G + AnS)	0	109.9	101.1
	12	108.9	99.2
	24	106.3	95.2
	Change from BL	–3.6%	–5.8%
		<b>P &lt; 0.01</b>	<b>P &lt; 0.01</b>

<sup>a</sup>Assuming proportionally distributed events in missing cases when calculating percentages.

<sup>b</sup>Equilibrated Kt/V was computed according to the double pool Daugirdas equation for arteriovenous and venovenous accesses. Blood samples were taken according to the European Best Practice Guidelines for Haemodialysis after a long interval of the respective dialysis regimen [9, 10].

<sup>c</sup>Relative mean change from baseline (BL) to month 24 (negative values denote a decrease).

In all other cases, odds ratios (ORs) were determined to compare relative differences without any time dependency. Time trends were investigated by performing conventional longitudinal analyses with maximum likelihood estimators to provide valid results in case of isolated missing values or dropouts classified as missing completely at random (MCAR) or missing at random (MAR), respectively. Life table analyses were performed for evaluation of mortality by applying Kaplan–Meier estimators and related plots. Different strata were compared with the log-rank test. In addition, death rates of the study population were

compared with data from the German Centre of Gerontology [Deutsches Zentrum fuer Altersfragen (DZA)] [14].

## Results

### Study population

A total of 2507 haemodialysis patients (45% female, 55% male) 19–98 years of age (median 70 years) in 76 private (for-profit) and 16 public (not-for-profit) dialysis centres were enrolled in the study.

The median haemodialysis vintage at baseline was 19.2 months (95% CI 17.6–20.8). A total of 20%, 68% and 12% of the study population were registered in the years 2004, 2005 and 2006, respectively. At each assessment after baseline, documentation was complete in 94% of cases (median value over complete study period) and for 63% of survivors at 24 months complete documentation for all study appointments ( $n=25$ ) was provided. FACIT scores were sampled in a subcohort of 1373 patients (55%).

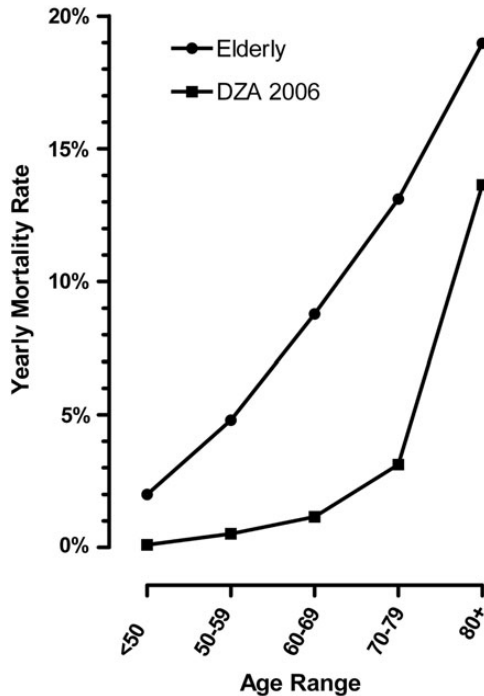


Fig. 1. Age-specific yearly mortality rate of haemodialysis patients in the ELDERLY study compared with the German background population (DZA: Deutsches Zentrum fuer Altersfragen). Detailed numbers are demonstrated at the bottom of Table 3.

Withdrawal occurred in 9.3% ( $n=232$ ) due to renal transplantation ( $n=92$ ), change of dialysis centre ( $n=52$ ), termination of RRT ( $n=25$ ), cessation of darbepoetin alfa therapy ( $n=25$ ) or other reasons ( $n=38$ ). The median follow-up time was 24.2 months.

### Baseline demographic data

At study entry, 1711 patients (68%) were <75 years and 796 (32%) were  $\geq 75$  years of age (median 66 and 79 years, respectively). At enrolment, the younger cohort showed a longer duration of RRT, a higher percentage of male patients and a higher frequency of native arteriovenous (AV) fistulas (see Table 1). The distribution of the age-adjusted CCI values is demonstrated in Table 3. The level of general nursing care was reported as degree 2 or 3 in 17.4 and 4.7% in the older and younger cohort, respectively.

### Mortality

The overall mortality rate in the 24-month observation period was 21.8% ( $n=547$ ), with rates of 34.7 and 15.8% for patients  $\geq 75$  and <75 years of age, respectively. The main causes of death were heart failure (23%), septicemia/infection (17%), myocardial infarction (10%), stroke (7.7%) and malignancies (6.0%). The median haemodialysis vintage at study enrolment did not differ substantially between survivors and non-survivors (18.8 versus 21.9 months, respectively) and was lower in the older patient cohort (see Table 1). The comparison with data from the national age-matched background population (DZA 2006 data) revealed an average difference in the yearly mortality rate of approximately +6–7% (absolute value) (17.4 versus 11.2% in the cohort  $\geq 75$  years and 7.9 versus 1.1% in the cohort <75 years) (see Figure 1) [14]. Consequently, the relative mortality risk for the younger haemodialysis population was disproportionately high (OR 8.4 for patients <75 years). The Kaplan–Meier estimate for the 24-month survival probability for elderly patients was 62.8%, compared to 82.9% for patients in the younger age group (log-rank test  $P < 0.0001$ ; see Table 3). No significant differences were observed regarding the survival probability of patients in private versus public dialysis centres (see Table 3). The mortality rate of patients with a CCI  $\leq 6$  was 14.7% (<75 years:

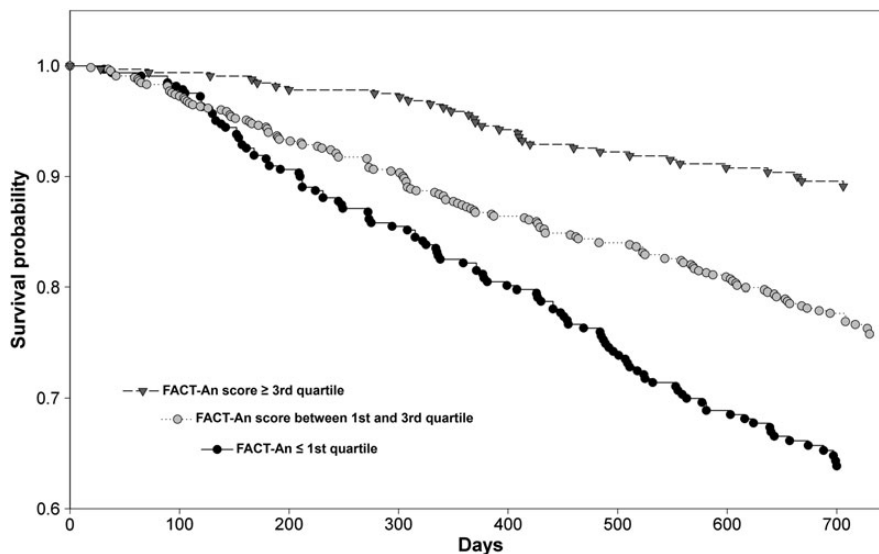


Fig. 2. Kaplan–Meier estimates for survival stratified by the baseline FACT-An score. The survival probability at the end of the observation period was 0.89, 0.78 and 0.64, respectively.



12.1%;  $\geq 75$  years: 24.9%) versus 34.5% for patients with a CCI  $\geq 7$  ( $< 75$  years: 27.0%;  $\geq 75$  years: 41.3%). Multivariate Cox regression analyses with the observation period as the target variable identified three variables that were associated with a mortality risk reduction: baseline Hb  $> 10$  g/dL [HR 0.8 (95% CI 0.6–1.0)] as well as a higher ( $> 1$ st quartile) body mass index (BMI) [HR 0.7 (95% CI 0.6–0.9)] and higher ( $> 1$ st quartile) FACT-An score [HR 0.7 (95% CI 0.6–0.9)]. Increasing age of patients  $\geq 75$  years [HR 1.7 (95% CI 1.3–2.3)], higher levels ( $> 1$ ) of nursing care [HR 1.3, (95% CI 1.1–1.6)], the presence of cardiovascular diseases [HR 1.5 (95% CI 1.1–2.0)] or a high range of comorbid conditions (CCI  $\geq 7$ ) [HR 1.5 (95% CI 1.1–2.0)] increased the mortality risk by at least 10%. Adding information from the QoL assessment (see Figure 2), the baseline FACT-An score was identified as a powerful predictor of survival probability [HR 0.7 for patients in the highest quartile (95% CI 0.6–0.9),  $P = 0.0004$ ].

### Hospitalizations

During the 24-month observation period, 33–34% of all patients were hospitalized at least once, with no substantial difference between the two age groups (see Table 3). In each time interval of 3 months at least one hospitalization occurred in 8.4% of all patients (average value of all visits). The median number of all-cause hospital days per patient-year for the total population was 9.7 (95% CI 8.6–11.0). Elderly patients were hospitalized for a median of 12.3 days (95% CI 9.7–15.6) compared with 8.9 days (95% CI 7.8–9.9) in the younger cohort (see Table 3). In 93% of all cases the duration of the hospital stay was  $< 30$  days.

### Quality of life

Limited self-care, which was defined as a general nursing care level  $> 1$  ( $> 1.5$  h of estimated support per day; see above) was present in 34% of patients  $\geq 75$  years of age and in 17% of patients in the younger cohort. The risk for an allocation to a care level  $> 1$  was more than twice as high for patients in the elderly cohort [OR 2.6 (95% CI 2.1–3.1)]. The QoL scores are demonstrated in Table 4 and Figure 3. A descriptive comparative analysis of the total patient population and the subgroup of patients with sampled QoL scores indicated the homogeneity of both groups with respect to age, gender, BMI, underlying disease, concomitant diseases, dialysis period, CCI and mortality. At baseline, the greatest differences between the two patient groups (in ascending order) were observed in the anaemia, physical and functional subscales. These three indices, reflected by the TOI score, also showed the greatest deterioration over the course of the observation period. The scores for EWB showed a moderate deterioration in both cohorts. Interestingly, the value for SWB was equal in both age groups at the end of the observation period due to a more pronounced decline in the younger cohort. The total score (FACT-An) decreased by 3.9% in 24 months ( $-3.6\%$  and  $-5.8\%$  for the younger and older cohort, respectively) and was  $\sim 10\%$  lower in the elderly subgroup at the end of the study period. To estimate the degree of independent information from each individual score, a pairwise correlation for the FACT-An score was performed. With the exception of the SWB subscale (Pearson correlation coefficient  $\rho = 0.46$ ), all scores showed a strong positive correlation ( $\rho \geq 0.80$ ), which was highest for the 20-item anaemia subscale ( $\rho = 0.93$ ) and the TOI ( $\rho = 0.97$ ).

### Treatment parameters and achievement of target levels

Vascular access using native vessels was used in 81.2% of patients  $\geq 75$  years of age versus 86.5% in the younger cohort (see

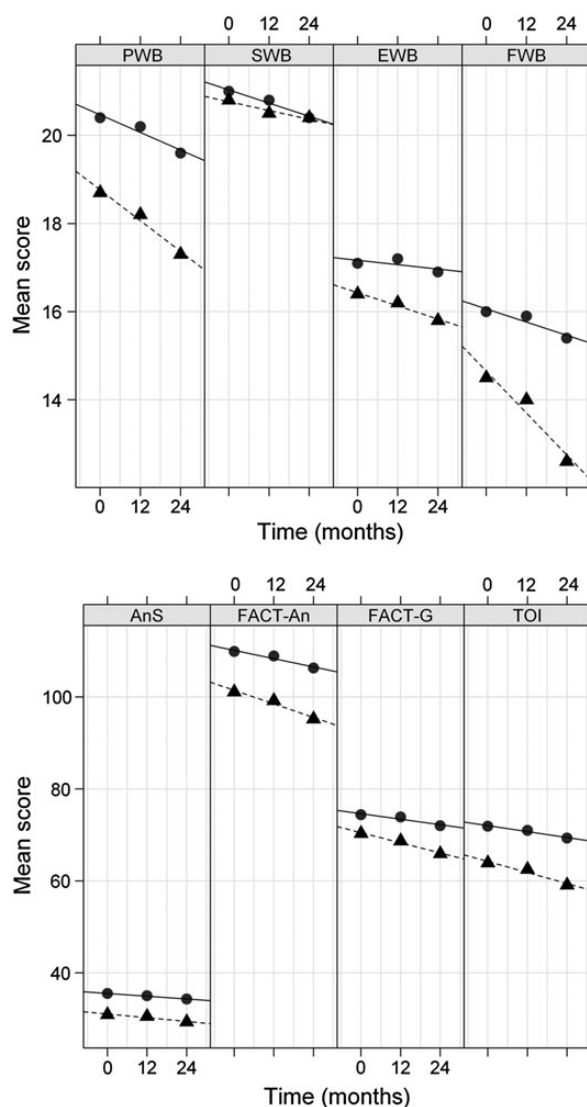


Fig. 3. Lattice plots of the QoL parameters (maximum likelihood estimates and regression line) at baseline, 12 and 24 months (filled circle:  $< 75$  years; filled triangle:  $\geq 75$  years).

Table 1), with rates of AV fistula thrombosis/occlusion of 2.2 and 3.2% per patient-year, respectively. The median administered darbepoetin alfa dose was 30  $\mu\text{g}/\text{week}$  and did not differ between the two age groups. The achieved Hb levels were stable (see Table 4). Transfusions were documented in 8.4% of the total study population over the course of 24 months (7.7% in the age class  $< 75$  and 10.1% in the age class  $\geq 75$  years). Dialysis adequacy slightly increased during the observation period in both cohorts. The serum albumin level remained stable during the course of the study for both age groups and was lower in the older cohort (see Table 4).

### Discussion

In recent years, the number of elderly patients with ESRD has steadily increased [1, 2]. There has been a discussion whether—compared with conservative management—dialysis improves the QoL in the elderly patient population, particularly because the survival benefit of commencing dialysis in this age group is

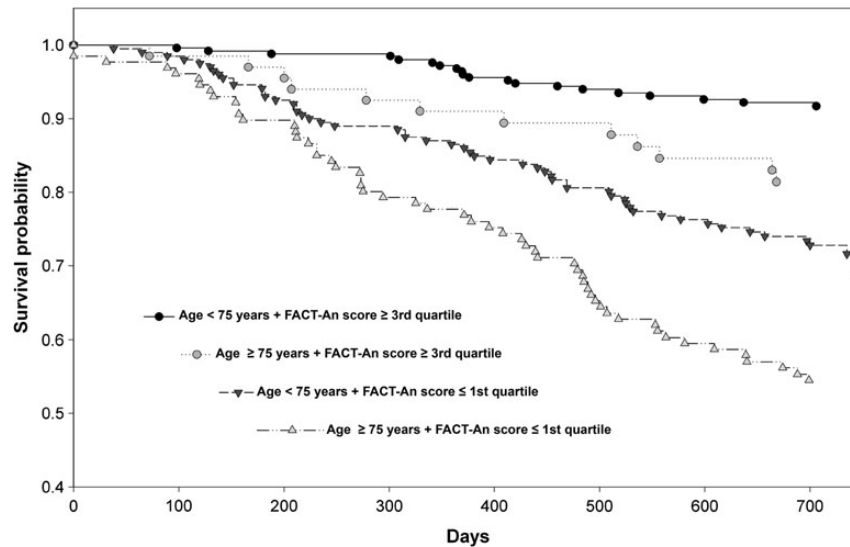


Fig. 4. Kaplan–Meier estimates for survival stratified for age and FACT-An score. The survival probability at the end of the observation period was 0.92, 0.81, 0.69 and 0.55, respectively.

often reduced as a result of the considerable comorbidity and factors such as late referral [15–20]. A recent European survey shows a rate for conservative care of up to 15% in elderly patients with terminal renal failure [21]. The presence of severe comorbidities (particularly vascular dementia) and a low physical-functional status were important factors to withhold RRT. Patient preference was a key criterion underlining the significance of shared decision making. In particular, frailty is associated with poor outcomes in haemodialysis patients [7, 22–24]. Also, favourable results have been reported, especially for patients participating in geriatric rehabilitation programmes [8, 25–29]. Another point of discussion is whether the additional lifetime gained by commencing haemodialysis in the elderly is considered rewarding by the patient [30, 31]. Hospital admissions, particularly if frequent and prolonged, impact all measured domains of QoL. Apart from emotional and social factors, hospitalizations are closely associated with further physical and functional deterioration, the need for long-term care and an increased mortality [24, 32]. In our study, the observed hospitalization rate (33–34% of patients in 24 months) did not differ significantly between the two age groups (see Table 3). The median yearly hospitalization time was—as expected—higher in elderly patients (12.3 versus 8.9 days/year), but lower compared with USRDS registry data [median of 15.5 days/year (adjusted); 2005 period prevalent patients ≥75 years] and considerably lower compared with some reports in the past (up to a median of 33.4 inpatient days per year of survival for patients ≥75 years of age) [1, 24]. Dialysis efficacy was high throughout the observation period and did not differ significantly between the two age groups or between treatments in private or public institutions. Contrary to the results of a study with USRDS data, no significant differences were observed with respect to mortality in private or public dialysis centres [33]. Three sessions per week was the standard therapy in elderly patients. While the prevalence of native arteriovenous fistulas is generally high in the European (and Japanese) dialysis population, this study also shows a high rate in the elderly patient cohort (>81%). The generally lower rate of native arteriovenous fistulas in elderly patients could be explained in part by the higher rate of native fistula failures due to the higher prevalence of diabetes and atherosclerotic disease [1, 34]. Current data suggest

that prosthetic grafts are an adequate approach to vascular access in this population, while catheter placement should still be considered a last resort [35, 36].

During the 24-month observation period there was no major clinically relevant deterioration of parameters considered relevant for survival, such as serum albumin, phosphate control and BMI. In addition to the adequate control of these critical biochemical and biophysical factors, the elderly haemodialysis patients showed a high degree of social well-being. While the EWB was in general lower and reduced to a greater extent in the elderly cohort, the SWB score was the same in both age groups at the end of the observation period and a more pronounced decline was observed in younger patients (see regression line in Figure 3). In accordance with previous findings, the physical and functional status deteriorated more sharply in the elderly cohort [37]. The change in performance status over time is well reflected by the TOI as a summary index containing the physical (PWB) and functional (FWB) as well as the symptom subscale scores (AnS) (see bottom of Figure 3). Prior studies have also shown that in particular the functional status of the elderly haemodialysis patient worsens notably despite treatment of uraemia, especially when significant comorbid conditions were present [7, 38]. On the other hand, there is evidence that an acceptable functional status can be maintained until the very late phase in conservatively managed elderly ESRD patients and that a palliative ‘no dialysis’ approach may be more suitable for a certain subset of patients [39, 40]. Murtagh et al. [41] reported 2-year survival rates of up to 66% for ESRD patients managed without RRT and that functional status declined steeply only in the last month of life.

The present study documents that the mortality rate of elderly haemodialysis patients was not exceedingly higher compared with the age-matched background population (absolute increase of the yearly mortality rate of 6.2% for the cohort ≥75 years; see Figure 1). The Kaplan–Meier estimate for survival at the end of the 24-month observation period was 62.8% for patients ≥75 years and comparable to the results reported for the European cohort in the Dialysis Outcomes and Practice Patterns Study III (prevalent patients 2005–2007) [42]. The adjusted 2-year survival rates for incident (and therefore non-selected) patients from



other registries are lower, as expected, and range from 54 to 59% [2, 18, 43]. A smaller study from Murtagh et al. [16] comparing elderly CKD stage 5 patients managed conservatively or with haemodialysis showed 2-year survival rates of 47 and 76%, respectively. The survival advantage of dialysed patients was lost in patients with a high level of comorbidity, especially among patients with ischaemic heart disease. A recent single-centre retrospective study showed no significant survival advantage among patients  $\geq 80$  years of age choosing RRT over a conservative approach [44]. Several parameters have been identified to be associated with a better survival of elderly patients on dialysis [18, 26, 45–49]. In the present study the survival probability was closely linked to the baseline 47-item FACT-An score (see Figure 2). A close correlation of the total FACT-An score with the anaemia subscale (AnS) containing 20 quickly assessable items was demonstrated (Pearson correlation coefficient  $\rho = 0.93$ ). Elderly patients with a high QoL had a higher survival probability than patients in the younger cohort with poor overall QoL (FACT-An  $\leq 1$ st quartile; see Figure 4). Although available in daily clinical routine, it is still a matter of debate whether to use predictive outcome models as part of clinical decision making.

The results from the current study are certainly limited due to its observational nature and the possible selection bias. All patients were on erythropoietin therapy and survived the crucial initiation period of haemodialysis. Consequently, this study cannot provide information on mortality in the early months after initiation of RRT (the median haemodialysis vintage was roughly 1.5 years) and all estimates concerning survival and QoL should only be regarded as an upper limit. Furthermore, patients with considerable frailty or cognitive impairment were less likely to be included, although the trial did not set up limitations with regard to comorbid conditions. Regarding the possible additional selection of healthier patients by sampling QoL parameters on a voluntary basis, the performed descriptive comparative analysis indicated that the QoL subgroup was representative of the total study population. The geographical distribution of centres did not show specific clusters. We considered the increasing number of missing values and dropouts as an important reason for bias and therefore determined point estimators with classification of missing values as MCAR and dropouts as MAR (see statistical section for details). Erythropoietin, which was administered to all study patients, does not seem to have a significant impact on QoL parameters according to a recent meta-analysis [50]. For a better reflection of age as an important predictor of death from a comorbid condition, the age-adjusted CCI was applied. Its use in ESRD patients has been validated [51]. As a restriction, the CCI does not consider non-malignant haematological conditions such as anaemia.

In conclusion, this study demonstrates that in-centre haemodialysis in the elderly can be associated with a mortality rate that was not exceedingly higher compared with the age-matched background population. The mean hospital days per year tended to be lower than previously reported for elderly haemodialysis patients and no major difference in the hospitalization rate was noted in comparison to the younger age group. While the social/family QoL in the elderly cohort was fairly stable and equivalent to the younger cohort at the end of the study period, a pronounced deterioration of performance status was noted. The baseline FACT-An score correlated closely with the survival probability at the end of the 2-year observation period. The decision making for or against dialysis should always be on a highly individual basis and chronological age alone should not be considered as the foundation. This underlines the growing importance of geriatric aspects in nephrology and the need for further studies in this field.

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## Conflict of interest statement

U.F. has been employed by Amgen® Germany, the sponsor of the study, since 1999. All other authors have no conflicts of interest in relation to the publication of this article.

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