Co-Morbidity rather than the Use of Hemodiafiltration Determines Mortality in a Contemporary West-European Dialysis Population

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Abstract

Background: *By using convective transport, hemodiafiltration (HDF) is more effective in removing larger uremic toxins (the so called middle molecules, such as β_2-microglobulin) than hemodialysis (HD). As these uremic toxins play an important role in the pathogenesis of atherosclerotic cardiovascular diseases in dialysis-patients, it is conceivable that HDF leads to a lower mortality and less cardiovascular events as compared to HD. We held a prospective observational trial in three Belgian dialysis centres, investigating the effect of online HDF on all-cause mortality, compared to high-flux HD.*

Methods: *In three Belgian dialysis centres, all patients receiving dialysis for at least six months up to a maximum of three years were selected. Hospitalized patients or patients with access-problems (possibly leading to inadequate dialysis) during the last three months were excluded. We registered their baseline characteristics (including Charlson Comorbidity Index), dialysis characteristics, biochemistry and medication (for all of which we calculated the mean in a period of three months before inclusion). Patients were monitored for a period of six years. The primary endpoint was all-cause mortality.*

Results: *We enrolled 242 patients (142 male, mean age 70,9 ± 10,3 years): 84 in the HD-group, 158 in the HDF-group. After 6 years, the incidence of all-cause mortality was significantly higher in the HD-group than in the HDF-group: 54 of 84 patients in the HD-group (64,3%), 70 of 158 patients in the HDF-group (55,7%) (P = 0,04). However, after adjusting for potential confounders (especially age, vascular access and Charlson Comorbidity Index), no statistically significant difference was detected between both treatment groups with regard to all-cause mortality (p = 0,45).*

Conclusion: *In a Western aged dialysis population, treatment with HDF did not improve all-cause mortality compared to high-flux HD. Mortality seems to be determined by comorbidity rather than by clinical practice patterns.*

Introduction

Aim

To assess the effect of on-line HDF on all-cause mortality, compared to high-flux HD in a contemporary West-European dialysis population.

We performed a prospective observational trial in three Belgian dialysis centres, investigating the effect of online HDF on the primary outcome all-cause mortality, compared to high-flux HD.

Methods

- **Study design :** multicenter, prospective, 6 year observational study
- **Inclusion criteria :**
  - adult (> 18 years) dialysis patients
  - time on dialysis : 6 to 42 months
  - 3 Belgian dialysis centres
- **Exclusion criteria :**
  hospitalisation or access problems last 3 months
- **Follow-up :** 6 years
- **Primary outcome :** all-cause mortality

Results

Inclusion of 242 patients: 84 HD – 158 HDF

Variable	High-flux HD	Online HDF	p-value
Number of patients	84 (34.7)	158 (65.3)	
Dialysis vintage (months)	17.0 [10.0 – 26.0]	22.0 [13.3 – 31.0]	***0.04***
Age	76.5 [68.0 - 80.0]	71.0 [61.3 - 78]	***0.01***
Male/Female	49/35 (58.3/41.7)	93/65 (58.9/41.1)	0,93
Weight (kg)	65.5 [55.3 – 75.0]	73.3 [61.5 -80.4]	***0.001***
Charlson comorbidity index	7.0 [6.0 – 9.0]	7.0 [5.0 – 8.0]	***0.02***
History of PTX	1 (1.2)	7 (4.4)	0,27
Primary renal diagnosis			0,46

Table 1. Characteristics of included patients at baseline. Data are presented as n (%) or median [interquartile range 25 – interquartile range 75].

Variable	High-flux HD	Online HDF	p-value
Hemoglobin (g/dL)	11.5 [10.8 – 12.4]	11.8 [11.4 – 12.1]	0.18
Calcium (mg/dL)	8.9 [8.5 – 9.2]	8.9 [8.4 – 9.2]	0.35
Phosphorus (mg/dL)	4.5 [3.9 – 5.1]	5.0 [4.4 – 5.6]	***< 0.001***
Calcium-phosphorus product	39.1 [33.8 – 45.2]	43.4 [37.4 – 50.5]	***0.001***
Phosphorus reduction rate (PRR)	59.8 [51.9 – 66.0]	60.0 [53.9 – 64.9]	0.82
PTH (ULN)	3.5 [2.0 – 4.3]	3.3 [1.8 – 5.5]	0.69
CRP (mg/dL)	0.6 [0.3 – 1.5]	0.6 [0.3 – 1.3]	0.55
Albumin (g/dL)	3.6 [3.2 – 4.0]	3.5 [3.3 – 3.7]	***0.07***

Table 2. Biochemical characteristics during the last three months before inclusion. Data are presented as median [interquartile range 25 – interquartile range 75].

Variable	High-flux HD	Online HDF	p-value
Hours dialysis/week	12.0 [10.6 – 12.0]	12.0 [10.5 – 12.0]	0.10
Mean blood flow Qb (ml/min)	299 [274 – 317]	327 [300 – 350]	***< 0,001***
Dialysate flow Qd (ml/min)	500 [500 – 500]	800 [500 – 800]	***< 0,001***
Convection volume (L/session)		20.2 [16.2 – 22.2]	-
Calcium dialysate (mmol/L)	1.5 [1.3 – 1.5]	1.5 [1.5 – 1.5]	***0.01***
Kt/V	1.5 [1.3 – 1.7]	1.5 [1.4 – 1.7]	0.25
URR	72.3 [67.0 – 76.8]	73.3 [69.2 – 77.3]	0.23
nPCR (g/kg/day)	0.9 [0.8 – 1.1]	0.9 [0.8 – 1.1]	0.62
Interdialytic weight gain (kg)	1.9 [1.0 – 2.4]	2.0 [1.1 – 2.6]	0.18
Access characteristics:			***0,003***
AV-fistula bipuncture	47 (56)	120 (75.9)	
AV-fistula unipuncture	7 (8.3)	4 (2.5)	
Central catheter	30 (35.7)	34 (21.5)	

Table 3. Dialysis parameters during the last 3 months before inclusion. Data are presented as n (%) or median [interquartile range 25 – interquartile range 75].

Variable	Number of patients		Daily dose		p-value
	HD	HDF	HD	HDF	
Ca-based binders	58 (69.0)	96 (60.8)	1.20 [0.80 – 1.60]	1.20 [0.80 – 1.60]	***0.05***
Non-Ca-based binders	11 (13.1)	47 (29.7)	0.59 [0.41 – 0.66]	0.58 [0.38 – 0.75]	***0.003***
Colecalciferol	51 (60.7)	82 (51.9)	246 [246 – 1035]	1087 [824 – 1087]	0.29
Alfacalcidol	38 (45.2)	69 (43.7)	1.75 [0.81 – 3.00]	2.42 [1.64 – 3.05]	0.77
Cinacalcet	2 (2.4)	3 (1.9)	75.0 [67.5 – 82.5]	9.6 [6.6 – 47.7]	0.79

Table 4. Doses of Ca-based and non-Ca-based phosphate binders (DDD*/day), colecalciferol (IE/day), alfacalcidol (µg/week) and cinacalcet (mg/day) during the last 3 months before inclusion. The number of patients that take this medication is presented as n (%). The dose is presented as median [interquartile range 25 – interquartile range 75].

**DDD is defined as Daily Defined Dose by the World Health Organisation (WHO). The DDD are: calciumcarbonate 3 g/day, calciumacetate 2g/day, sevelamer 6,4 g/day, lanthanum carbonate 2,25 g/day.*

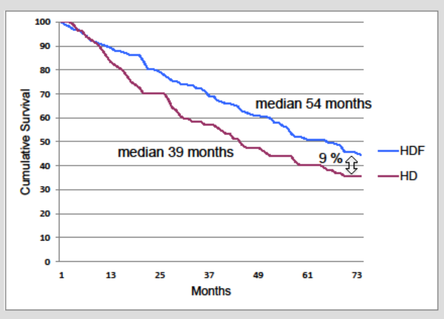

Figure 1. Kaplan-Meier survival curves for time to death from any cause in patients treated with HDF and high-flux HD.

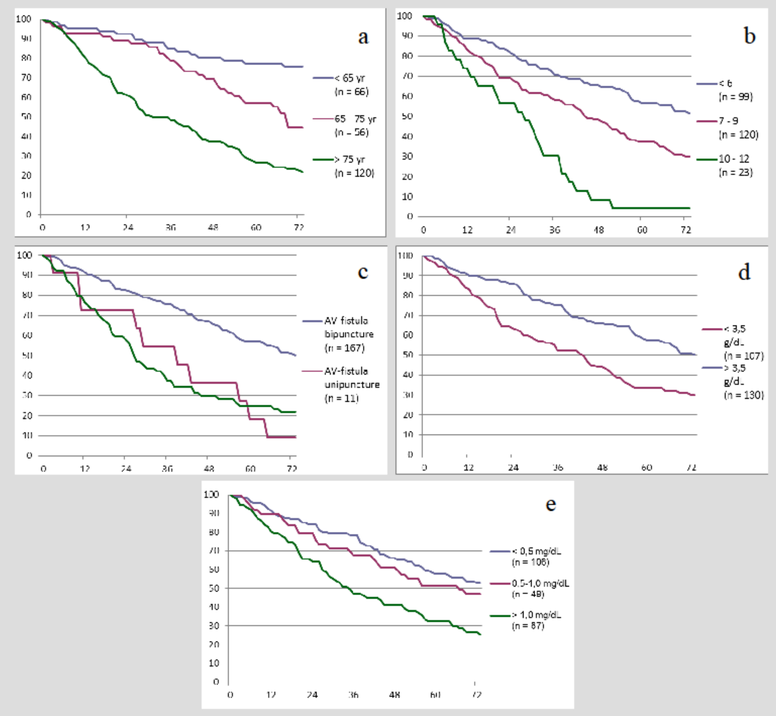

Figure 2. Kaplan-Meier survival curves for time to death from any cause in patients in correlation with age (a), Charlson Comorbidity Index CCI (b), vascular access (c), albumin (d) and C-reactive protein CRP (e). (n = number of patients in each group).

Variable	HR	95% CI	p-value
Age	1.03	1.01 – 1.06	***0.003***
Charlson Comorbidity Index CCI	1.30	1.16 – 1.45	***< 0.001***
Weight	0.98	0.97 – 0.99	***0.02***
Ca-concentration of dialysate	3.60	1.06 – 12.24	***0.04***
Vascular access	1.43	1.19 – 1.72	***< 0.001***
Interdialytic weight gain	1.31	1.07 – 1.61	***0.009***
Albumin	0.61	0.39 – 0.97	***0.04***

Table 3. Multivariate analysis on survival (Cox proportional hazards model). Only hazards ratios showing a significant result are presented.

Discussion

Although univariate analysis showed better survival in patients treated with HDF as compared to those treated with HD, this effect was overruled in multi-variate analysis by the combined effects of age, CCI, dry weight, calcium concentrate of the dialysate, vascular access, interdialytic weight gain and serum albumin.

Substantially older population than those studied in earlier trials (mean age 70,9 years).

Mean convection volume 20,2 L/treatment, similar as in other trials. Reflects daily clinical practice in an older dialysis population (limitations of vascular access and Qb).

Conclusion

In a contemporary West-European dialysis population, we did not see a survival benefit of HDF over high-flux HD after correction for confounding variables.

Variables reflecting co-morbidity (age, CCI, vascular access) rather than clinical practice patterns were found to play the most important prognostic role.

53 ERA 409--SP

Dialysis. Extracorporeal dialysis: techniques and adequacy.

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DOI: 10.3252/pso.eu.53era.2016

ePosters supported by F. Hoffmann- La Roche Ltd.

53rd CONGRESS ERA-EDTA VIENNA AUSTRIA MAY 21st-24th, 2016 Held jointly with Österreichische Gesellschaft für Nephrologie

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