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Original Article

Outcome of home haemodialysis patients: a case-cohort study

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Abstract

Background. Randomized, controlled comparisons between home haemodialysis (HHD) and centre haemodialysis (CHD) have not been performed to date. Reported survival benefits of HHD as compared with CHD from uncontrolled studies have been attributed largely to patient selection.

Methods. In order to minimize a selection bias, we have compared the outcome of our HHD and CHD patients with a nested case-cohort study. For each patient trained for HHD at our dialysis centre between 1970 and 1995 ($n = 103$), a corresponding match was searched from the CHD patients by retrospective chart analysis. The pairs were matched for sex, age (±5 years), time of dialysis therapy onset (±2 years) and renal disease category. For 58 of the 103 HHD patients, a corresponding matched CHD patient was identified. Both treatment groups had the same mean age (50 ± 13 years) at dialysis onset and were comparable with respect to the Khan comorbidity index, prevalence and duration of hypertension, smoking habits, history of myocardial infarction, stroke and peripheral vascular disease. In both groups, ~50% of the patients were transplanted during the observation period.

Results. HHD patients were hospitalized less often and tended to have fewer operations as compared with CHD patients. Survival was significantly longer in HHD as compared with CHD. Five, 10 and 20 year survival rates were 93 ($n = 55$ patients at risk), 72 (41) and 34% (11) with HHD and 64 (38), 48 (26) and 23% (4) with CHD, respectively. This survival difference persisted after adjusting for predictors of mortality, i.e. age at onset of dialysis, year of start of dialysis therapy and Khan comorbidity index.

Conclusions. HHD offers a cheap and valuable alternative to CHD, with no apparent disadvantages.

Keywords: case-cohort study; home haemodialysis; survival

Introduction

For ~40 years home haemodialysis (HHD) has been recognized as a possible alternative to renal replacement therapy at a dialysis centre (CHD). HHD started in Japan in 1961 [1,2], and became available in Boston in 1963 [2] and 1 year later in London [2]. The first patient to start HHD in Switzerland did so in 1964. He was a mountain guide who had been trained in London [3].

Today, the predominant renal replacement therapy modality in Switzerland is CHD. The maximum incidence of HHD was reached in 1977 when 15% of all the patients on dialysis started treatment by this modality [3]. While there were still ~12% of the patients treated by HHD in 1986 [3], a steady decline of the number of patients on HHD down to 29 patients (<3%) (March 2003) was observed thereafter. A similar decline in the number of patients treated with HHD during the last years was observed in most countries. In the United States, the incidence of HHD therapy dropped from 40% in the early 1970s to 0.5% in 2000 [4]. Today, relevant numbers of patients treated with HHD are reported only from Australia (17%) and New Zealand (16%) [5].

Part of the decline in incidence numbers of HHD has been attributed to the rapid rise of peritoneal dialysis [2,6]. Interestingly, the use of peritoneal dialysis has also started to diminish in many Western countries. The current decrease of home dialysis methods is probably mainly due to socio-economics and, possibly, to medical reasons. The end-stage renal disease (ESRD) population became older with a higher fraction of diabetic and polymorbid, disabled patients. In addition, more for-profit units were established, which traditionally do not encourage HHD [2]. In Switzerland, a further obstacle is the difficulty to recruit relatives willing to assist HHD patients.

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Besides transplantation, HHD has been reported to provide the best quality of life, most independence and the best working rehabilitation for ESRD patients [2]. Apart from the above-noted medical and social benefits, HHD offers a great economic advantage: in Switzerland the annual cost of HHD is estimated as sFr 54 000 compared with sFr 78 000 for CHD. There have even been reports of a substantially lower mortality with HHD compared to either CHD or continuous ambulatory peritoneal dialysis (CAPD) [7]. Analyses of survival by modality are complicated by non-random assignment to treatment modalities and, further, when patients are treated with sequential modalities. The reported differences in survival between HHD and CHD patients have often been attributed to selection bias [8]. HHD patients in general differ from patients treated in medical facilities with respect to age, race, sex and cause of ESRD, all factors with significant impact on survival [7,9]. In general, HHD patients are younger, less frequently have diabetes mellitus as a cause of ESRD, are more likely to be white and men, and have a higher socio-economic status and a more stable family life.

The current study compared patients on HHD with CHD patients matched for gender, time and age at onset of dialysis as well as for primary renal disease, with a follow-up over 20 years. The intention was to analyse whether the better survival rate reported with HHD was due to haemodialysis modality.

Subjects and methods

Patient selection

All patients starting HHD at the University Hospital of Berne between 1970 and 1995 were identified. These 103 patients comprised all patients starting HHD in the district of Berne. None of the other dialysis facilities in the district trained patients for HHD during this period.

For each dialysis patient treated at home, a corresponding match was searched from the haemodialysis patients treated in the centre during the same period by retrospective chart analysis. Each matched pair of patients had to have the same sex and age (±5 years), to start haemodialysis treatment at the same time (±2 years) and to have the same underlying cause of renal disease causing ESRD (i.e. glomerulonephritis, pyelonephritis, analgesic nephropathy, Polycystic kidney disease, renal vascular disease, unknown). Patients eligible for matching were treated by haemodialysis for ≥3 months prior to any change of renal replacement therapy. Intermittent peritoneal dialysis for ≤1 month was accepted. Patients treated at any time by HHD or self-care dialysis were excluded as possible matches for the HHD treatment group. When more than one possible match was available for any HHD patient, the one CHD patient who started dialysis treatment at a time-point closest to the corresponding HHD patient was selected.

Retrospective chart analysis of the HHD and the CHD patients was done by two independent persons. Matching was done prior to the data analysis of the HHD patient group and was not changed thereafter.

The stringent matching criteria described above allowed the selection of only 58 of the 103 HHD patients for comparison with a corresponding match from the CHD population. The 58 matched HHD patients did not differ from the total population of 103 HHD patients with respect to marital status, sex, age, renal diagnosis, year and age at dialysis onset, employment status and the comorbid conditions mentioned below.

Data collection

Data collected included patient identifiers (age, sex and marital status), renal diagnosis, information concerning year of dialysis onset, age at dialysis onset and information concerning last employment status. The presence or absence of a variety of comorbid conditions before onset of dialysis was recorded. These comorbid conditions were history of cigarette smoking, diabetes mellitus, treatment of hypertension, myocardial infarction, cerebrovascular or peripheral vascular disease, tuberculosis and chronic obstructive pulmonary disease.

Follow-up data included morbidity and mortality during the dialysis period, including operations, hospitalizations and date of death or transplantation.

Analytical methods

Only the matched 58 pairs of patients were used for further analysis.

Due to the number of cases, most of the data being categorical and the non-normal distribution of the continuous data, we chose non-parametric methods of statistical analysis. Since this was a survey of paired data, we used the Sign test or the Friedman two-way analysis of variance when comparing multiple variables between cases and control.

Comorbidity was scored using the Khan comorbidity index [10]. This index, derived from patient age and number of comorbidities, has been shown to be appropriate to express the prognostic impact of comorbidity on mortality risk in patients with ERSD [10].

Survival time was defined as the time from the initiation of the first dialysis treatment until death from any cause or the last date of follow-up alive. Survival plots were done using the Kaplan–Meier estimation. The initial comparison of the two groups was performed using the log-rank test. After univariable analysis, possible predictive factors (treatment modality, gender, smoking status, marital status, Khan comorbidity index and renal disease) were entered into a multivariable Cox proportional hazards model. Insignificant variables were eliminated using a backward elimination procedure.

All statistical analyses were performed with the software Systat 10 (SPSS Inc., NY, USA) on a personal computer.

Results

Basic patient characteristics of both groups are given in Table 1. Two-thirds of both groups were male. The majority of patients in both groups were married, but the proportion tended to be higher in HHD than CHD (84% *vs* 70%). Both populations were comparable with respect to the proportion of smokers, history of

Table 1. Basic patient characteristics at the start of haemodialysis treatment

	HHD	CHD
n	58	58
Male (%)	39 (67%)	39 (67%)
Married (%)	55 (84%)	41 (70%)
Year of dialysis onset (SD)	1983 (6.3)	1983 (6.6)
Age at dialysis onset (years) (SD)	50.1 (13.5)	50.6 (13.1)
Diabetes (%)	0 (0%)	1 (1.7%)
Smokers (%)	16 (27.6%)	20 (34.5%)
History of myocardial infarction (%)	3 (5.2%)	4 (6.9%)
History of cerebrovascular disease (%)	1 (1.7%)	3 (5.2%)
History of peripheral arterial disease (%)	2 (3.4%)	3 (5.2%)
Tuberculosis	3 (5.2%)	4 (6.9%)
COPD (%)	7 (12.1%)	7 (12.1%)
Khan comorbidity index		
Low risk	50 (86%)	43 (74%)
Medium risk	3 (5%)	10 (17%)
High risk	5 (9%)	5 (9%)

COPD, chronic obstructive pulmonary disease.

myocardial infarction, cerebrovascular and peripheral arterial disease, chronic respiratory illness, age and year of dialysis onset.

Primary renal disease was a matching variable and, therefore, did not differ between the two groups. Diagnoses included in each group were glomerulonephritis 18 (31%), pyelonephritis 9 (16%), analgetic nephropathy 18 (31%), ADPKD 9 (16%) and renal vascular disease 3 (5%). There was one patient in each group with a renal disease of unknown origin.

Patients with relatively benign overall prognosis were prevalent in both groups (Table 1) and no difference with respect to the distribution of the Khan comorbidity index between the two groups was observed (Table 1). There was neither a difference with respect to the mean duration of hypertension nor to the high percentage of patients treated for arterial hypertension between the two groups (Table 2). Six patients treated in-centre were hepatitis B antigen-positive as compared with two patients treated at home (not significant). About half of the patients from both groups were transplanted during follow-up (Table 2).

The same dialysis treatment parameters and time prescriptions were used at home and in the centre. Mean weekly treatment times were 9.5 ± 1.9 h/week at home and 9.4 ± 2.6 h/week in the centre, with 2.5 ± 0.4 and 2.3 ± 0.5 treatments per week, respectively. Estimates of urea reduction rates were available from 45 patient pairs ($63 \pm 6\%$ *vs* $61 \pm 7\%$).

About half of the patients of each group remained employed during dialysis (Table 2). Neither the number of employed patients nor the mean percentage of work ability differed between the two groups (Table 2). HHD patients tended to work more often in technical or farming occupations, respectively, as compared with CHD patients who more often did office work.

Table 2. Patient characteristics during the study

	HHD	CHD
Employ [*n* (%working ability ± SD)]	28 (41.8 ± 36.2%)	26 (35.0 ± 35.8%)
Learned profession [*n* (%)]		
Technical/farming	28 (48.3%)	21 (36.2%)
Home	9 (15.5%)	10 (17.2%)
Office	19 (32.8%)	26 (44.8%)
Working as [*n* (%)]		
Technical/farming	22 (37.9%)	12 (20.7%)
Home	17 (29.3%)	16 (27.6%)
Office	17 (29.3%)	27 (46.6%)
Hepatitis B antigen-positive	2 (3.4%)	6 (10.3%)
Hypertension [*n* (%)]	45 (77.6%)	51 (87.9%)
Mean duration of hypertension ± SD (years)	13.7 ± 10.0	11.5 ± 11.5
Transplanted during study time (*n*)	28	31

Table 3. Morbidity during dialysis defined as event (*n*) per patient

	HHD	CHD
Hospitalizations total	6.3[a]	10.5
Dialysis-associated problems	1.0[a]	2.3
Uncontrolled hypertension	0.3	0.4
Uraemia-related	0.1[a]	0.8
Vascular problems	1.2[b]	2.0
Abdominal problems	0.3[a]	1.0
Gynaecological/urological	1.4	1.7
Cardiac problem	0.5	0.7
Bleeding	0.1	0.1
Social reasons	0.05[b]	0.5
Operations total	6.4	8.8
Parathyroidectomies	0.2[a]	0
Laparatomies	0.3[a]	0.7
Cholecystectomies	0.05	0.1
Appendectomies	0.1	0.3
Sigmoidectomies	0.02	0.1
Bleeding complications	0.09	0.05
Cataract	0.1	0.1
Gynaecological/urological	1.7	2.5
Cardiac	0.05	0.03
Vascular access	2.5	3.9
Carpal tunnel syndrome	0.3[a]	0.05

Data are number per patient.
[a] $P < 0.001$ and [b] $P < 0.05$, as compared with CHD.

CHD patients were more likely to be hospitalized, mainly due to dialysis-related problems, such as uraemic symptoms or volume overload (Table 3). Furthermore, CHD patients were more often hospitalized for 'social' reasons as compared with HHD patients. No differences were found between the two groups with respect to hospitalizations for uncontrolled hypertension, complications of bleeding, access operations or cardiac problems.

CHD patients had more abdominal problems and they had a higher rate of cholecystectomies and

laparatomies (Table 3). Furthermore, there was a tendency for more sigmoidectomies and appendectomies in the CHD patient population. CHD patients had more vascular problems, i.e. complications of peripheral arterial disease, angina and myocardial infarction. The proportion of parathyroidectomized patients was higher in the group of HHD patients (Table 3). HHD patients were also more often operated for carpal tunnel syndrome (Table 3).

About half of the patients from each group died during the observation period (Table 4). The leading causes of death in both populations were cardiovascular diseases followed by infections and cerebrovascular insults in the CHD patients. Two patients of the HHD group died of air embolism and another two discontinued dialysis treatment. In ~9% of cases, the cause of death was not specified.

Survival time was significantly longer in HHD as compared with CHD. Five, 10 and 20 year survival was 93 ($n = 55$ patients at risk), 72 (41) and 34% (11) with HHD and 64 (38), 48 (26) and 23% (4) with CHD, respectively. Predictors of mortality identified by a multivariate Cox proportional hazard model in the population studied were age at onset of dialysis ($P < 0.001$), year of onset ($P < 0.001$), Khan comorbidity index ($P < 0.05$) and treatment method ($P < 0.05$). The survival difference for treatment methods persisted after adjustment for the other predictors of mortality. The main cause of death was from cardiovascular disease in both groups (25.9% for HHD and 22.4% for CHD patients). HHD patients were significantly less hospitalized (6.3 *vs* 10.5 times per patient) and tended to have fewer operations (6.4 *vs* 8.8 per patient) as compared with the CHD patients.

If stratified for primary renal disease, there were significant differences concerning survival (log-rank test: $P < 0.003$), with patients having glomerulonephritis living the shortest time (median survival: 8.4 years) and those with interstitial nephropathy the longest (median survival: 16.7 years). Patients with ADPKD had a median survival time of 12.9 years and those with renal vascular disease 11 years.

Table 4. Mortality during dialysis

	HHD	CHD
Total number of deaths during the study	29 (50%)	34 (58.6%)
Causes of death		
Cardiovascular disease	14 (24.1%)	12 (20.7%)
Malignant disease	1 (1.7%)	4 (6.9%)
Infection	1 (1.7%)	6 (10.3%)
Gastrointestinal haemorrhage	0 (0%)	1 (1.7%)
Cerebral insult	0 (0%)	4 (6.9%)
Air embolism	2 (3.4%)	0 (0%)
Suicide	1 (1.7%)	1 (1.7%)
Dialysis	2 (3.4%)	0 (0%)
Other	3 (5.2%)	2 (3.4%)
Unknown	5 (8.6%)	4 (6.9%)
Mean follow-up ± SD (years)	10.5 ± 5.4	7.4 ± 5.7

Discussion

From 1970 to 1995, a total of 103 patients started HHD therapy in our centre. Fifty-eight of these patients could be matched with patients that were concomitantly treated in the dialysis facility according to time of dialysis onset, age, gender and primary renal disease. Survival analysis revealed a benefit of HHD as compared with CHD with respect to 5, 10 and 20 year survival rates. These findings were confirmed by the use of a stepwise multivariate Cox proportional hazard model, where dialysis modality emerged as the second most important mortality predictor after patient age.

The findings of our study are well in accordance with earlier reports of a survival benefit of patients treated by HHD [7–9,11]. Using a Cox proportional hazards model and a national random sample of patients starting ESRD treatment in 1986 and 1987, adjusted for age, race, sex, diabetes as cause of renal disease and comorbid factors present before onset or ESRD, Woods *et al*. [8] reported a relative mortality risk of 0.58 for patients treated with HHD as compared with CHD. The authors speculated that the observed survival benefit of HHD was due to an increased compliance with medication, diet and dialysis prescription. They could not exclude a selection bias with respect to HHD patients having less severe abnormalities in coronary artery, cerebral and peripheral vascular disease and other unmeasured comorbid conditions. Reported survival data from the major HHD studies are summarized in Table 5. The rather low patient survival of the only unselected HHD population [5] hints at the importance of patient selection on reported survival rates.

A randomized, controlled trial to compare HHD with CHD is impossible for obvious reasons. Patients cannot be randomized to HHD treatment, as it requires the capability as well as the willingness of the patient to participate. We focused on a strict match of our HHD patients to the centre population, considering sex, age (±5 years), year of haemodialysis onset (±2 years), renal diagnosis (i.e. glomerulonephritis, pyelonephritis, analgesic nephropathy, ADPKD, renal vascular disease and unknown). Hence, the two studied populations were comparable with respect to the mentioned criteria. Furthermore, the comorbidity index [10] was comparable in both populations.

Due to the strict matching process, for only 50% of the HHD patients was a suitable match found in the CHD population. Furthermore, neither the selected HHD patients nor their matched patients from the dialysis centre were any longer representative of their corresponding population. The main reason for the small number of patients that could be matched was the strategy of our institution to consider pre-emptive transplantation, HHD, self-care dialysis or CAPD rather than passive CHD as a preferred choice for young patients. Despite the fact that one of the HHD patients was diabetic, no diabetic patient was found

Table 5. HHD survival data as reported from the literature

Authors	Observation period	Number of patients	Mean age (years)	Survival (%)							
				1 Year	2 Years	3 Years	4 Years	5 Years	10 Years	15 Years	20 Years
Moorhead *et al.* [21]	1964–1970	89	–	99	93	91	86	–	–	–	–
Roberts [22]	1967–1973	981	40	87	74	62	54	52	–	–	–
Delano [23]	1969–1996[a]	206	40	Mean survival: 6.4 ± 6.4 years							
Mailloux *et al.* [9]	1970–1993	74	44	–	–	–	–	87	60	47	35
McGregor *et al.* [5]	1970–1979	92[b]	42	–	83	–	–	57	–	–	–
	1980–1989	127[b]	46	–	80	–	–	56	–	–	–
	1990–1997	115[b]	50	–	88	–	–	75	–	–	–
Weller *et al.* [24]	1974–1978	261[c]	43[d]	86	75						
Arkouche *et al.* [25]	1974–1997	552	31–53	–	–	–	–	90	77	62	45
Hellerstedt *et al.* [26]	1978–1983	148	54	94	86	75	64	64	–	–	–
Grant *et al.* [11]	1982–1988	139	39	–	–	–	–	71	–	–	–

[a]Publication year (end of observation period not given).
[b]Unselected HHD population (no CHD available).
[c]Including 29 patients treated with peritoneal dialysis.
[d]Estimated value.

as a match in the passive CHD population as self-care dialysis patients were excluded.

HHD requires the help of a partner. Active patients lacking a steady partnership are therefore not trained for HHD, but are trained for an alternative active dialysis method, i.e. peritoneal dialysis or self-care haemodialysis. It is therefore not astonishing that more married persons were found in the group of HHD patients. A certain impact of this inhomogeneity on patient mortality cannot be excluded, especially since married people have been reported to have a longer survival time.

Two-thirds of the studied patients were male. While female patients are not *per se* underrepresented in the population with active dialysis treatment (i.e. self-care haemodialysis and peritoneal dialysis), a certain disadvantage of female patients is observed as soon as they require the help of their partner. The same phenomenon can be observed for the gender distribution of nursing homes.

The observed difference in the type of occupation between HHD and CHD in our study was not surprising. HHD requires some manual skills from the patients and, therefore, patients used to manual work are easier convinced to do the dialysis treatment themselves than white-collar workers. Furthermore, farmers living in remote areas gain more time by HHD as compared with patients living in a city close to a dialysis facility.

While the observed overall survival was different between HHD and CHD patients, there was no striking difference with respect to the cause of death, with cardiovascular disease being the major reason for dying (Figure 1). This corresponds well to some published data [12], while it is in discordance with others [13]. The additional number of deaths observed in the CHD patients occurred mainly during the initial month of dialysis therapy and, therefore, we cannot postulate a sustained survival advantage of HHD. It is not possible to exclude a higher initial degree of comorbidity in the CHD patients. Furthermore, patients originally planned for future treatment at home who died before or during the HHD training in the hospital were not counted as HHD patients.

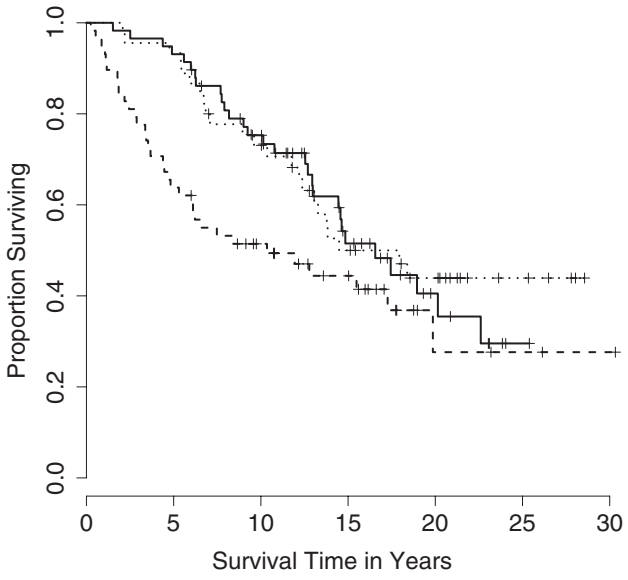

Fig. 1. Proportion of the matched patients surviving on HHD (solid line) or CHD (dashed line) during the observation period. The dotted line represents the survival of the 45 HHD patients who could not be matched. The observed survival times of censored patients are marked '+'.

CHD patients tended to die more frequently from malignancies, strokes and infections. However, it is likely that in the HHD population, where more people died at home as compared with the centre dialysis patients, death from cardiac disease was more often declared by the family practitioner as compared with death declarations from the treating nephrologist being fully aware of all concomitant diagnoses of the patient. Two patients of the HHD group died of air embolism.

This is a well-known danger of HHD that has been described previously [14].

Patients dialysed in the centre were hospitalized more often than HHD patients. This can be explained easily for dialysis-related problems, since centre patients are already dialysed in the hospital and see their physician thrice weekly as compared with about every 6 weeks for stable home dialysis patients. However, higher frequencies for hospitalizations related to abdominal problems as well as the number of laparatomies were also higher in CHD – a circumstance with no obvious explanation.

More parathyroidectomies and operations for carpal tunnel syndrome were done in the HHD patients. One might speculate that calcium and phosphate levels were less rigorously controlled at home, possibly due to compliance problems. Carpal tunnel syndrome in dialysis patients has been associated with the type of membrane [15] used for dialysis as well as the quality of dialysate [16]. While we used the same dialysis filters at home as in the centre (cuprophane before 1989 and, exclusively, biocompatible membranes in recent years) we cannot exclude the possibility of an inferior water treatment at home, at least during the early years of HHD. Furthermore, the differences encountered with respect to carpal tunnel syndrome might also be attributable to work-related factors [17].

Efficiency of dialysis was rather low as compared with today's standards (urea reduction rate 63 and 61%, respectively). The mean weekly dialysis treatment time of <12 h is given mainly by the fact that several patients were treated only twice a week. Patients were treated differently in the past; however, our HHD patients had conventional treatment schedules during all eras, i.e. comparable to the patients treated in the centre.

The observed decrease of patients starting HHD has been attributed partly to the increased frequency of transplantation in the young and selected population of HHD patients. In our study, both patient groups were transplanted with the same frequency invalidating the argument that patients are either treated at home or transplanted.

Except for Australia and New Zealand [4,5], the number of HHD patients has been declining steadily over the last decades. Elder and sicker patients, greater mobility of patients and better distribution of dialysis centres have all contributed to the decline in the number of home dialysis patients. Furthermore, reimbursement policies often disadvantage the physician and their patients, which themselves tend to prefer the 'real medicine' delivered at a dialysis centre [2].

HHD may become more attractive again with the emergence of new therapy schedules, such as daily haemodialysis and/or overnight haemodialysis. Reports about dialysis patients treated with such treatment schedules are encouraging with respect to patient morbidity [18,19] and/or mortality [20]. However, investigations that focus on the separation of the 'home effect' from a possible advantage of the treatment modality *per se* are needed, especially if such modalities are accompanied by an increased need for financial and/or human resources.

Considerable patient selection occurs during the decision process about which renal replacement therapy to choose. Patients on HHD are a selection of healthier and younger patients with better rehabilitation profile [8]. As HHD requires a considerable commitment of time and effort by the patients and their family, one could speculate that this population is more compliant with medication, diet and dialysis prescription, hence achieving a higher dose of dialysis (Kt/V) [8]. Even if attributing the observed survival benefit of HHD treatment to persistent problems with matching the two populations, we found no negative effect of HHD on any of the studied parameters. This finding together with possible advantages for the patients treated at home in combination with a financial profit for the society should be reasons enough to continue convincing and training patients for HHD.

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