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Patients' perspective of haemodialysis-associated symptoms

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Abstract

Introduction. Patients often report symptoms during haemodialysis (HD). To better understand patients' experience, we surveyed routine HD outpatients, to quantify the burden and duration of dialysis-associated symptoms.

Methods. Five hundred and eight symptom questionnaires were returned from 550 HD outpatients (92.4%). The symptoms in relation to the HD session were analysed using a visual analogue score. Multivariate logistical regression analysis was used to identify characteristics associated with total symptom burden and time to recover following a HD session.

Results. Fifty-four percent of the cohort were male, median age 64 years, 36% diabetic and median age unadjusted Charlson comorbidity score 3.0 (2–5). Fatigue (82%), intradialytic hypotension (76%), cramps (74%) and dizziness (63%) were the commonest symptoms reported, followed by headache (54%), pruritus (52%) and backache (51%), with fatigue occurring with a median frequency of 50% of dialysis sessions and intradialytic hypotension and cramps in 30%. Some 23% reported recovering from dialysis within minutes, 34% by the time they returned home, 16% by bed time, 24% the following morning and 3% just before the next dialysis session. Symptom burden was associated with female sex, younger age, longer duration of dialysis sessions, ethnicity and dialysis centre practice. The time taken to recover from dialysis varied from minutes to hours and was shorter for men and greater dialysis vintage but longer with increasing session time and those with increased intradialytic symptom burden.

Conclusions. Despite advances in HD, intradialytic symptoms were frequently reported by our patients. There was substantial unexplained variation in symptom burden across centres, suggesting that clinical practice or policies may play a role in preventing the adverse effects of dialysis. Symptom burden was worse in women, patients of South Asian as opposed to African origin and also in those receiving a longer duration of dialysis. These patients may therefore benefit from a different approach to dialysis prescription.

Keywords: fatigue; hypotension; intradialytic symptoms

Introduction

Over the last 40 years, haemodialysis (HD) has moved from a specialized treatment for a selected minority, in university-associated hospitals in North America and Europe, to an accepted routine outpatient treatment, with increasing numbers of patients now treated outside hospital

in free-standing dialysis centres, without on-site medical supervision.

Patients with chronic kidney disease, Stage 5, who opt for conservative management rather than dialysis [1], are usually polysymptomatic typically reporting lack of energy, 76%; pruritus, 74%; drowsiness, 65%; dyspnoea, 61%; peripheral oedema, 58%; pain, 53%; dry mouth, 50%; muscle cramps, 50%; restless legs, 48%; lack of appetite, 47%; poor concentration, 44%; dry skin, 42%; sleep disturbance, 41% and constipation, 35% [2]. However, despite the introduction of regular HD treatments, many patients remain symptomatic [3, 4]. Just as with those patients who opt for conservative management of their chronic kidney disease, patients on HD typically experience multiple symptoms, with pain, fatigue, pruritus and constipation present in >50% [3]. The most commonly reported potentially treatable symptoms include bone and joint pains, insomnia, mood disturbance, sexual dysfunction, paraesthesia and nausea [4].

Although there are many studies addressing quality of life of patients with end-stage kidney disease, there are very few studies that have specifically looked at patient symptoms directly attributable to the HD procedure. As there have been many technological advances and improvements in HD over the last 30 years [5], we wished to establish the burden and duration of dialysis-associated symptoms in a diverse cohort of patients currently dialysed in a variety of outpatient settings, under the care of a tertiary referral centre. Furthermore, we attempted to characterize patient and dialysis factors associated with these outcomes.

Methods and patients

Thrice weekly HD outpatients under the care of a tertiary referral centre were asked to complete a visual analogue score of both a range of symptoms specifically experienced during the HD session (back ache, chest pain, cramps, dizziness post-dialysis, fatigue, headache, hypotension, nausea, palpitations, pruritus, shortness of breath and vomiting), the frequency of symptoms (Score 10 = symptoms present during each dialysis session to 0 = never experienced symptoms) and also the time taken to recover from dialysis. These questionnaires had been developed internally from experience with previous patient perspective surveys of treatment quality [6–11], with intradialytic hypotension [12] referring to dizziness due to low blood pressure or nursing interventions to treat hypotension during dialysis.

Patients were dialysed in six different care settings, ranging from a dialysis unit within the National Health Service (NHS) tertiary referral unit to satellite centres based either within an NHS acute general hospital or community hospital, in a private not for profit hospital and in free-standing for-profit centres and a small number dialysing at home. All dialysis centres had a trained dialysis nurse to patient ratio of 1:4 and used 0.9–1.0 L of 0.9% saline as priming solution, and machines were both heat and chemically cleaned between patients. Patients were dialysed using polysulphone dialysers (FX series; Fresenius, Bad Homburg, Germany) [13] and low-molecular weight heparin as the standard anticoagulant. Dialysate water quality met current UK chemical and bacteriological standards.

As the number of home dialysis patients was small, for the purposes of centre analysis, these patients were excluded. The reference centre, Centre 1, is an NHS unit-based in a community hospital with regular specialist medical input but no direct access to radiology, haematology or biochemistry services. Centre 2 is an NHS satellite unit based in an acute general hospital, without full-time specialist cover but receiving specialist input several times per week. Centre 3 is an NHS hospital-based HD unit associated with a tertiary referral renal unit with full-time specialist medical cover. Centre 4 is an NHS unit based in an acute general hospital with on-site specialist medical cover available most days. Centre 5 represents patients from two for-profit community-based satellite dialysis units with regular specialist medical input but no on-site radiology, haematology or biochemistry services. Centre 6 represents a private hospital-based non-profit satellite dialysis unit with regular specialist medical input. All dialysis shifts were visited at least monthly by a supervising accredited renal specialist.

Ethical approval for the study was granted as part of audit and service development, in keeping with a UK Department of Health directive to survey patient satisfaction with NHS treatments.

Statistical analysis

Except where otherwise stated, results are expressed as mean ± SD, median and interquartile range, or percentage. Statistical analysis was by chi-square test corrected for small numbers (or Fisher's exact test where expected cell numbers were <5) along with *t*-test and analysis of variance (or Mann–Whitney *U*- and Kruskal–Wallis tests for non-normally distributed variables) for continuous variables. For analysis of between centre effects, subjects undergoing home dialysis were excluded ($n = 12$) and patients dialysing at the two for-profit centres run by the same company were combined (to avoid small cell numbers) as staff and policies were identical. To identify independent associations with symptom burden, the arithmetic sum of symptom scores was determined. Symptom burden and duration were examined in multivariate logistical regression (ordinal logistic regression for symptom burden scores), which was undertaken with Stata version 11. Initially, the model included diabetes, Charlson comorbidity index [14], end stage renal failure (ESRF) duration and dialysis centre, sex and race (as we hypothesized these factors might impact on symptoms *a priori*). Other demographic dialysis and comorbidity variables (Tables 1 and 3) were then entered into the model one at a time in a step-wise fashion. Variables were only retained in the model where the 95% confidence intervals (CIs) for the estimate did not include zero or there was an improvement in model fit (as demonstrated by the −2 log likelihood). Statistical significance was taken at or <5% level.

Results

Five hundred and eight questionnaires were returned from 550 patients (92.4%), 53.6% male, median age 64 (60–74.5) years, 36.3% diabetic and median dialysis vintage 37 (18–64) months. Patients came from a range of ethnic origins 45.1% white, 29.3% black, 20.3% South Asian subcontinent and 2.2% other racial groups. The Charlson comorbidity scoring system [14] was used to classify patient comorbidity, and the age unadjusted Charlson comorbidity score was calculated, median 3.0 (2–5), with 23.96% of patients having had a previous myocardial infarction (MI), coronary artery bypass surgery or coronary artery angioplasty and stenting, 14.2% previous cerebrovascular disease, 12.4% peripheral vascular disease (PVD) and 5.5% previous peptic ulcer disease (PUD) [14].

Median weight predialysis was 71 kg (60.3–82.9 kg) and postdialysis 69 kg (58.8–81.0 kg), with a median weight loss of 1.8 kg (1.2–2.4 kg) and median percentage weight loss of 2.6% (1.8–3.4%). The median duration of the dialysis session was 4 h (range 2.5–5.25 h) and median dialysate sodium 138 (136–138) mmol/L. Median dialysate calcium 1.35 mmol/L (1.25–1.35 mmol/L), all dialysates had a magnesium of 0.5 mmol/L and glucose 1 g/L. Most patients dialysed with a blood flow of 800 mL/min but 109 (21%) dialysed with a lower blood flow, typically 500 mL/min. Two hundred and eight (49%) patients dialysed against a dialysate of 35°C with the remaining dialysing against warmer temperatures. All patients used steam sterilized polysulphone dialysers (FX series; Fresenius) median

Table 1. Patient and dialysis factors stratified by symptom burden category[a]

	Low $n = 159$	Moderate $n = 176$	High $n = 169$	OR (95% CI)
Symptom score				
Score, median (IQR)	7 (3–11)	22 (17–27)	44 (37–54)	
Sex*				
Female, *n* (%)	61 (38)	78 (44)	92 (54)	1.38 (1.11–1.72)
Age years, mean (SD)	63.3 (17.1)	61.7 (15.5)	59.5 (15.6)	
Racial group[#]				
White, *n* (%)	87 (55)	69 (39)	73 (43)	0.81 (0.65–1.00)
Black, *n* (%)	45 (28)	60 (34)	47 (28)	0.98 (0.75–1.22)
South Asian, *n* (%)	24 (15)	36 (20)	36 (21)	1.24 (0.94–1.61)
Other, *n* (%)	3 (2)	11 (6)	12 (7)	1.67 (1.04–2.77)
Diabetes, *n* (%)	55 (35)	62 (35)	65 (38)	1.10 (0.88–1.38)
Target weight, kg, mean (SD)	69.9 (15.6)	70.3 (16.2)	72.3 (18.4)	
PVD, *n* (%)	19 (12)	12 (7)	26 (15)	1.19 (0.85–1.68)
PUD, *n* (%)	4 (3)	6 (3)	13 (8)	1.82 (1.08–3.06)
MI, *n* (%)	41 (26)	36 (20)	36 (21)	0.88 (0.68–1.14)
CVA, *n* (%)	21 (13)	23 (13)	23 (14)	1.1 (0.74–1.40)
Duration of dialysis session[††], h, median (IQR)	4 (3.5–4)	4 (4–4.35)	4 (4–4.25)	
Mean dialysate sodium[†], mmol/L, median (IQR)	137 (136–138)	138 (137–138)	138 (137–138)	
Dialysate flow rate <800 mL/min, *n* (%)	30 (19)	33 (19)	36 (21)	1.07 (0.82–1.39)
Dialysate temperature*** >35°C, *n* (%)	64 (40)	94 (53)	98 (58)	1.42 (1.15–1.77)
Dialysis weight change, kg, median (IQR)	1.7 (1–2.2)	1.9 (1.25–2.5)	1.9 (1.3–2.5)	
Duration of ESRF, months, median (IQR)	36.5 (11.5–74)	37.5 (19–67)	37 (19–64)	
Charlson comorbidity score				
Score, median (IQR)	4 (2–5)	3 (2–5)	3 (2–5)	
Centre[‡]				
1, *n* (%)	23 (14)	43 (24)	43 (25)	1.38 (1.06–1.79)
2, *n* (%)	22 (14)	23 (13)	25 (15)	1.04 (0.76–1.42)
3, *n* (%)	60 (38)	27 (15)	11 (7)	0.37 (0.28–0.49)
4, *n* (%)	21 (13)	32 (18)	46 (27)	1.55 (1.19–2.05)
5, *n* (%)	13 (8)	24 (14)	32 (19)	1.58 (1.14–2.16)
6, *n* (%)	17 (11)	20 (11)	10 (6)	0.75 (0.52–1.09)

[a]Values expressed as either mean (SD) or median [interquartile range (IQR)]. Home dialysis patients excluded for analysis of centre. Where parameters have several categories, the odds ratios (OR) and 95% CI refer to the association between each category within that parameter and symptom scores. CVA, cerebrovascular accident.
*$P < 0.05$ by χ^2 test for trend, **$P < 0.01$ by χ^2 test for trend, ***$P < 0.005$ by χ^2 test for trend, [‡]$P < 0.005$ by χ^2 test, [#]$P < 0.05$ by Fisher's exact test, [†]$P < 0.05$ by Kruskal–Wallis test, [††]$P < 0.01$ by Kruskal–Wallis test.

dialyser surface area 1.8 m^2 (1.8–2.2 m^2). Patients were anticoagulated with low-molecular-weight heparin, tinzaparin (Leo Laboratories, Ballerup, Denmark), median dose 2500 IU (range 0–5000), administered into the venous limb of the dialysis circuit [15].

Dialysis adequacy was assessed by urea reduction ratio, median 75.5% (70.7–79.2), and single-pool *Kt*/*V*, median 1.65 (1.44–1.86). The bone profile included serum calcium, median 2.28 mmol/L (2.17–2.41); phosphate 1.49 mmol/L (1.22–1.84); serum calcium phosphate product of 3.45 $mmol^2/L^2$ (2.74–4.27) and parathyroid hormone 26.9 pmol/L (12.5–50.5).

Fatigue was the commonest symptom reported by 81.5% of patients surveyed, followed by intradialytic hypotension 76.4%, cramps 74.3%, dizziness post-dialysis 63%, headache 53.6%, pruritus 52.2%, backache 51%, nausea 34.5%, dyspnoea 32.5%, palpitations 26.8%, chest pain 24.8% and vomiting 23.1%.

Patients were asked to report the frequency of these symptoms, using a visual analogue scale, and again fatigue was the most common symptom, followed by intradialytic hypotension and cramps (Figure 1).

Just under a quarter of patients reported that they felt recovered, back to their baseline within a few minutes of ending dialysis, and around a third felt recovered by the time they reached home, whereas almost a quarter only felt better the morning after a dialysis session and just <4% of patients had only just recovered by the time they were due to return for the next dialysis session (Figure 2).

To further characterize patient and HD factors associated with the burden of symptoms on dialysis, individual patient symptom scores were summed. As patient symptom reporting was skewed, for analytical purposes patients were therefore divided into tertiles of a low (159 patients), moderate (176 patients) and high (169 patients) burden of symptoms. On univariate analysis, parameters found to

Table 2. Multivariable analysis of symptom severity adjusted for duration of ESRF, unadjusted Charlson co-morbidity index, dialysate flow and mean dialysate sodium concentration and age[a]

	OR (95% CI)
Sex***	
Female	2.22 (1.50–3.28)
Age* for each additional year	0.99 (0.97–1.00)
Race**	
White	Reference
Black	0.63 (0.39–1.00)
South Asian	1.54 (0.93–2.55)
Other	1.66 (0.74–3.70)
Duration of dialysis** for each additional hour	1.78 (1.16–2.74)
PUD**	3.54 (1.47–8.51)
Centre***	
1	Reference
2	0.76 (0.41–1.41)
3	0.21 (0.11–0.38)
4	1.52 (0.88–2.66)
5	3.34 (1.08–10.35)
6	0.71 (0.32–1.59)

[a]Home dialysis patients excluded (pseudo R^2 0.11). The P-values refer to the significance of the parameter overall (i.e. whether racial group is associated with outcome) in the model of symptom burden. Where variables have several categories, the odds ratios (OR) and 95% CI refer to the association between each category within that parameter and symptom score.
*P < 0.05, **P < 0.01, ***P < 0.005.

Table 3. Patient and dialysis factors stratified by time to recover from dialysis[a]

	Immediate $n = 120$	Delayed $n = 382$	OR (95% CI)
Sex**			
Female, *n* (%)	41 (34)	190 (50)	1.9 (1.2–2.9)
Age years, mean (SD)	60.2 (16.6)	61.9 (16.0)	
Racial group			
White, *n* (%)	59 (49)	170 (45)	0.89 (0.59–1.34)
Black, *n* (%)	40 (33)	112 (29)	0.86 (0.55–1.35)
South Asian, *n* (%)	15 (13)	80 (21)	1.45 (0.84–1.35)
Other, *n* (%)	6 (5)	20 (5)	1.04 (0.41–2.70)
Diabetes, *n* (%)	41 (34)	140 (37)	1.12 (0.73–1.72)
Target weight, kg, mean (SD)	71.3 (15.5)	70.7 (17.2)	
PVD, *n* (%)	11 (9)	46 (12)	1.35 (0.67–2.71)
PUD, *n* (%)	2 (2)	21 (5)	3.43 (0.78–14.9)
MI, *n* (%)	28 (23)	85 (22)	0.86 (0.52–1.41)
CVA, *n* (%)	13 (11)	54 (14)	1.35 (0.71–2.58)
Duration of dialysis session†, h, median (IQR)	4 (3.875–4.0)	4 (4.0–4.25)	
Mean dialysate sodium, mmol/L, median (IQR)	138 (136–138)	138 (137–138)	
Dialysate flow rate* <800 mL/min, *n* (%)	31 (26)	67 (17)	0.61 (0.38–0.98)
Dialysate temperature >35°C, *n* (%)	62 (52)	193 (51)	0.96 (0.63–1.44)
Dialysis weight change, kg, median (IQR)	1.75 (1.1–2.4)	1.8 (1.3–2.4)	
Duration of ESRF, months, median (IQR)	33.5 (15–68)	37.5 (18–68)	
Charlson comorbidity score			
Score, median (IQR)	3 (2–5)	3 (2–5)	
Centre			
1, *n* (%)	21 (18)	88 (23)	1.41 (0.83–2.40)
2, *n* (%)	13 (11)	56 (15)	1.41 (0.74–2.69)
3, *n* (%)	28 (23)	70 (18)	0.74 (0.45–1.21)
4, *n* (%)	21 (18)	78 (20)	1.21 (0.71–2.06)
5, *n* (%)	20 (17)	48 (13)	0.72 (0.41–1.27)
6, *n* (%)	13 (11)	34 (9)	0.80 (0.41–1.58)

[a]Where variables have several categories, the odds ratios (OR) and 95% CI refer to the association between each category within that parameter and delay in recovery. Values expressed as either mean (SD) or median [interquartile range (IQR)]. CVA, cerebrovascular accident.
*P < 0.05 by χ^2 test, **P < 0.01 by χ^2 test, †P < 0.05 by Kruskal–Wallis test.

Table 4. Multivariable analysis of time to recover following dialysis session adjusted for racial group, centre, unadjusted Charlson comorbidity index, age and mean dialysate sodium concentration[a]

	Odds ratio (95% CI)
Sex**	
Female	2.46 (1.48–4.08)
Duration of dialysis*** for each additional hour	2.68 (1.58–4.57)
Duration of ESRF* for each additional month	0.99 (0.98–1.00)

[a]Home dialysis patients excluded (pseudo R^2 0.07).
*P < 0.05, **P < 0.01, ***P < 0.005.

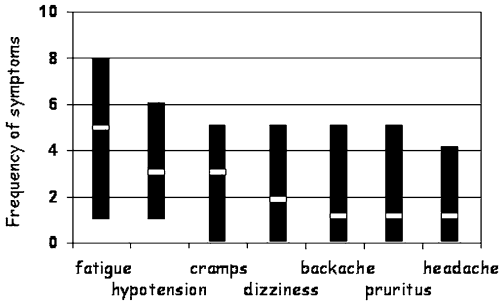

Fig. 1. Frequency of dialysis symptoms using visual analogue scale (Score 10 = symptom present during each dialysis session and Score = 0 symptom always absent). Most common symptoms. Values expressed as medians (white bar) and 25–75% confidence limits (black box).

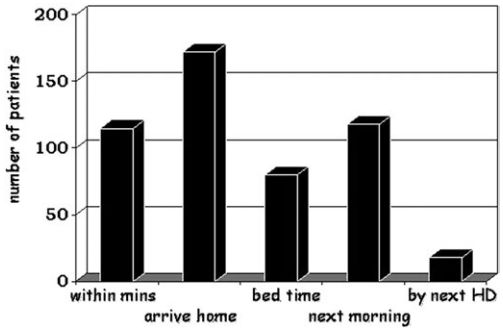

Fig. 2. Time to recovery following a HD session.

be significantly associated with burden of symptoms were female sex, racial origin, duration of dialysis session, dialysate sodium concentration, history of PVD and dialysate temperature, but patient age, diabetes, Charlson comorbidity score, cardiovascular comorbidity, weight change, post-dialysis weights and dialysis vintage showed no such association (Table 1).

In the multivariable model, patient age, duration of dialysis session, sex, racial origin, previous history of PUD and also dialysis centre were associated with symptom burden scores (in a model that also included duration of ESRF, comorbidity index, dialysate flow rate and mean dialysate sodium; Table 2). Higher dialysate temperature, although associated with symptom burden on univariate analysis, was dropped from the multivariable model as there was a strong relationship between this variable and both dialysis session time and dialysate sodium levels such that inclusion did not improve model fit. To explore the possibility of the association between racial group and symptoms being worse in women, a further exploratory analysis was carried out with a racial group × sex interaction term. This term did not improve the model fit and provided no evidence for effect modification.

As the time to recover post-dialysis was also skewed, patients were divided into two groups, those with early (119 patients) and delayed (382 patients) recovery. There was a strong relationship between dialytic symptom burden and time to recovery (P < 0.001). The two factors, which were most significantly associated with delayed recovery from dialysis, were female sex and longer duration of the dialysis session (Table 3). There was a strong relationship between symptom burden and delayed recovery (odds ratio: 2.86, 95% CI: 2.22–3.69 of delayed recovery for each unit increase in symptom burden category). On logistical regression analysis, the time for patients to recovery post-dialysis was shorter for males, those dialysing for shorter session times and patients with longer dialysis vintage (in a model that also included racial group, dialysis centre, comorbidity index and dialysate sodium concentration; Table 4). High dialysate flow rate was no longer associated with delayed recovery on multivariable analysis.

Discussion

Despite what appears to be satisfactory small solute clearances with a median urea reduction ratio of 75.5% and online Kt/V of 1.65, the majority of our patients reported multiple symptoms occurring during their dialysis session. Whereas many studies have reported on symptoms in patients with chronic kidney disease, treated by haemo-or peritoneal dialysis or those conservatively managed, very few studies have actually looked at symptoms specifically related to the dialysis treatment itself. We designed this survey to obtain information to help provide accurate information to help inform those patients who are approaching end-stage kidney disease along with members of the multidisciplinary chronic kidney disease care team. The symptom questionnaire was developed over time by studying patient responses to previous internal audit questionnaires [6–10].

The commonest symptom reported with dialysis was one of fatigue or general lethargy, followed by intradialytic hypotension, cramps and dizziness at the end of the dialysis

session. These symptoms could be explained by too rapid ultrafiltration rates for the rate of plasma refilling, leading to relative intravascular hypovolaemia [16]. Symptoms were more common in those patients dialysing with higher dialysate sodium concentrations (>140 mmol/L) on univariate analysis but this effect was not seen on multivariate analysis and this may represent reverse causation or confounding. For example, supervising clinicians selected a higher dialysate sodium concentration for those who experience symptoms or are at risk for other reasons of dialysis-associated complications (such as intradialytic hypotension) [17]. Fatigue and lethargy could also be associated with mild cerebral oedema, which can occur during HD due to too rapid urea clearance, creating osmotic gradients [18]. However, there was no relationship with increasing intradialytic weight loss, higher averaged ultrafiltration rates, blood flow rates or dialyser surface area. Similarly, symptom reporting was not increased in diabetic patients or those with previous history of MI or CVD.

Headache was reported by just over 50% of patients, in keeping with other studies [19]. Typically, headache occurs after 3–4 h of dialysis [20], although some believe that it is nitric oxide mediated [21], which is often initially generated at the start of the dialysis session. However, headache can also be associated with raised intracranial and intraocular pressures. One earlier study also reported an association between longer dialysis session times and headache, with increased symptomatic headache when patients had their treatment times increased from 4 to 5 h, despite decreased intradialytic hypotension [22].

Itching during dialysis was reported by ~50% of patients. Pruritus is a very common symptom in chronic kidney disease patients and has many potential causes [23, 24]. Although itching could be due to contact sensitization linked to vascular access cleansing solutions and needles [25] or reactions to components of the extracorporeal circuit [26], it could also be simply due to the patient being relatively immobile for several hours during dialysis and being unable to distract themselves, so become more aware of their generalized pruritus. Similarly, the increased reporting of backache could be related to relative immobility in a dialysis chair for several hours, in patients with underlying renal muscle and bone disorders [22].

On multivariable analysis, female sex, younger age, racial group, history of previous PUD and dialysis centre were all found to be associated with increased symptom reporting during dialysis. Women are typically smaller than men and examining the coefficients of the patients of South Asian subcontinent origin, who are more likely to be vegetarian and typically smaller than those of African origin [27], had higher symptom scores than those of African origin. However, we could not identify any association between reported symptom burden and post-dialysis weight, so body mass itself is unlikely to explain our findings. Previous studies have suggested that symptom perception in patients with chronic kidney disease may differ between ethnic groups [28] and also patients suffering from depression, the prevalence of which may also vary between patients of different origin, tend to report more symptoms [29]. The older patient is more likely to suffer from systolic hypertension and be at risk of intradialytic hypotension due to blunted autonomic compensatory responses, so it is interesting that older patients reported less symptoms in our study, although there was no association between post-dialysis blood pressure and age. Whether older patients have lower expectations in terms of quality of life and are more acceptant of and therefore report fewer symptoms with HD remains to be determined. On univariate analysis, there was an association between a dialysate temperature of >35°C and a history PVD with increased symptom burden. Cooler dialysates have been reported to improve cardiovascular stability during dialysis [30] and as such may be expected to help reduce symptom reporting. Patients with PVD may be more prone to cramps. However, on multivariate analysis, dialysate temperature, dialysate sodium and PVD were no longer independently associated with intradialytic symptoms. The effects of cooler dialysate in the univariate analysis could have been abrogated in the multivariate analysis due to linkage between other dialysis practices. We also identified an independent association between history of PUD and dialysis-associated symptoms but the very small numbers with this condition in our cohort mean this finding should be interpreted with caution.

There was also a difference in symptom reporting between centres, although centre practices, in terms of dialysis machines, dialysers, dialysate water quality and nursing complement, were very similar. There were differences between centres in terms of clinical practice, with variations of modal dialysate temperature and sodium, and ability to provide longer dialysis session times. However, the differences in reported symptom burden and dialysis centres persisted even when adjusted for differences in patient demographics, including sex, age, ethnicity and comorbidity and dialysate sodium concentration, and dialysate temperature. However, medical supervision varied between centres, from full-time access to doctors training in nephrology at the tertiary centre, ~50% of the time in the centre based at the NHS community hospital, to only emergency medical cover available in the other hospital-based dialysis units. The fewest symptoms were reported from patients dialysing in those centres with the most frequent direct medical contact. Whether increased medical contact per se or whether there are complex relationships between dialysis centre, physician and dialysis prescription that were not identified using our approach requires further investigation.

Just over half of our patients reported that they had recovered from dialysis by the time they reached home, but almost a quarter of patients only felt recovered the following day, and a small minority only felt better when it was time to return for the next dialysis session. Patients who took longer to recover post-dialysis typically reported more symptoms during the dialysis session. The delay in the time to recover post-dialysis was again more pronounced in female patients and those dialysing for longer session times, even when correcting for intradialytic symptom burden, and is in keeping with previous studies [22]. More recent studies have reported that the time to recover post-dialysis is shortened by shorter but more frequent dialysis sessions [31], suggesting that these effects are related to the cerebral effects of HD and may similarly be reduced by slow but continuous dialysis treatments [32]. On multiple

regression analysis, dialysis vintage was also shown to be associated with recovery time, suggesting that with the passage of time patients may adapt to these changes or perhaps that patients who recover more rapidly are willing to persist with dialysis therapy.

This study shows that although HD has progressed to a routine outpatient treatment in stand-alone satellite centres, many patients report symptoms during dialysis and take time to recover from the dialysis session. As doctors spend less time reviewing patients in outlying dialysis centres, the frequency of symptoms is often under estimated by clinicians [33] and as such mainly left untreated [3]. In our population, women and those from the South Asian subcontinent rather than African origin were more likely to suffer during and after dialysis, especially if dialysing for longer session times, raising the possibility of too rapid a clearance of urea. Although we could not exclude an effect of educational background and symptom reporting, we think that this is unlikely as there was no association between ethnicity and female sex and symptom reporting. Similarly, although patients suffering from intradialytic morbidity may have their dialysis session time increased, the main driving force determining session duration in our practice is achievement of urea clearance, as dialysis facilities have limited capacity. Furthermore, there were significant differences between centres, suggesting that there may be modifiable factors, which can significantly alter patient symptom burden. A better understanding of the causal nature of the associations with burden and duration of symptoms will allow the provision of renal replacement therapy, which is more acceptable to the expanding population with ESRF. This is the largest study of patient symptoms directly attributable to modern day outpatient HD treatment. As with any study based on patient questionnaires, there is always the question of validity of patient responses [11]. However, the strength of this report is due the high level of patient participation (>90%) and the wide spectrum of patients in terms of age, comorbidities and ethnic variation.

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