Established in 1871
Swiss Medical Weekly
Formerly: Schweizerische Medizinische Wochenschrift
The European Journal of Medical Sciences

Original article | Published 22 February 2013, doi:10.4414/smw.2013.13750
Cite this as: Swiss Med Wkly. 2013;143:w13750

Frequency and severity of pain and symptom distress among patients with chronic kidney disease receiving dialysis

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Summary

QUESTION UNDER STUDY: Data on pain management in haemodialysis patients with end-stage renal disease are scanty. Our study aimed to collect information on the frequency and severity of pain and symptom distress among long-term dialysis patients in southern Switzerland.

METHODS: Patients with chronic kidney disease stage 5, on dialysis, treated in five nephrology units in southern Switzerland, who had given informed consent and were able to complete the survey, were interviewed to assess pain and correlated symptoms using a Visual Analogue Scale (VAS), the Brief Pain Inventory and the Edmonton Symptom Assessment System. To evaluate the impact of symptoms, the Instrumental Activities of Daily Living questionnaire was used.

RESULTS: One hundred and twenty-three patients, aged 36–90 years and with a mean time on dialysis of 3.5 years, were interviewed. Pain was experienced by 81 patients during the 4 weeks before the interview: 68 had chronic pain; 66 reported pain intensity higher than 5 on the VAS; 35 identified musculoskeletal pain as the most disturbing pain. Five patients used drugs to cope with pain during the night. Asthenia and fatigue were prevalent concomitant symptoms. Asthenia, fatigue, sleep disturbances, dyspnoea, loss of appetite, nausea/vomiting and anxiety were correlated with pain. The majority of the patients reported that their pain limited their daily life activities.

CONCLUSIONS: Pain severity and symptom distress in dialysis patients are important, but underestimated and undertreated. They interfere with sleep quality and daily living. Routine assessment of pain burden, pain management similar to that used in palliative care, and adequate analgesic use to treat specific dialysis-associated pain syndromes should be considered in guidelines.

Key words: *analgesic; dialysis; pain; palliative care; quality of life; symptom burden*

Question under study

The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" [1, 2]. Pain is a common problem in patients with end-stage renal disease (ESRD) [2, 3], including dialysis patients [4–6], and may be due to their primary disease, concurrent comorbidity or disease following renal failure.

Dialysis therapy is life-saving, but underlying systemic diseases and related painful syndromes such as ischaemic limb, musculoskeletal or neuropathic symptoms persist during treatment. Recent reviews show that 47% of patients with ESRD experience pain [7] and this can be moderate to severe in 82% [5]. Pain often coexists with depression, anxiety and insomnia. Almost two of every five dialysis patients experience troubled sleep, and 38% to 45% suffer some degree of anxiety [7]. Symptom severity in dialysis patients has been reported in some studies to be comparable to that of cancer and HIV patients [4–6].

The complex pharmacokinetics of analgesics in dialysis patients often entails under-treatment of the symptoms [5, 8–11], and may hamper safe and effective use, especially of opioids [12].

Nephrologists often view as priorities dialysis access, management of bone metabolism, anaemia, and quality of dialysis. During the last few years, renal units predominantly

focused on dialysis parameters such as blood pressure, anaemia, intact parathyroid hormone (iPTH), Kt/V and on interventions aiming to minimise disease progression, rather than on symptom management. In general, individual pain symptoms are poorly recognised and managed [13–16], although their management should be an integral component of patient care quality. Previous studies have demonstrated that nephrologists commonly underestimate the symptom burden of individual patients [9, 17].

This study aimed to assess the prevalence, severity, cause and management of pain, together with associated symptoms and overall symptom burden, in patients with chronic kidney disease stage 5, on long-term dialysis and living in southern Switzerland.

Methods

Selection of patients

Inclusion criteria for this cross-sectional, observational, multicentre study were: chronic kidney disease (CKD) stage 5 according to the Kidney Disease Outcome Quality Initiative (K/DOQI) Guidelines [18]; chronic haemodialysis; treatment in one of the five nephrology units in southern Switzerland; age older than 18 years; ability to complete a questionnaire in Italian and to give informed consent. The local ethics committee approved the study and each participant gave written informed consent to participate.

Assessment of clinical data and symptoms

Basic demographic data and clinical laboratory data (such as liver and renal function, Kt/V values, electrolytes, complete blood count and C reactive protein) were collected from medical and nursing charts. Two palliative-care nurses interviewed the patients face-to-face at home or during a dialysis session, following a duly prepared grid. Patients were asked to complete the Brief Pain Inventory (BPI), in order to describe pain and associated symptoms relevant to chronic dialysis patients [19]. They were also asked to score the maximum pain experienced during the previous 4 weeks on a 10-cm visual analogue scale (VAS) ranging from "no pain" to "unbearable pain", in which mild pain ranged from 0–4, moderate from 5–7 and intense from 8–10. Patients were also asked to localise the pain and draw the location on a body diagram. Use of analgesics and drug prescriptions were recorded. Patients were then asked to complete the Edmonton Symptom Assessment System (ESAS) [20–25], used in palliative care as well as for dialysis patients [23], in order to assess the overall symptom burden. The Instrumental Activities of Daily Life (IADL) questionnaire [26] was chosen to quantify restrictions in daily life activities.

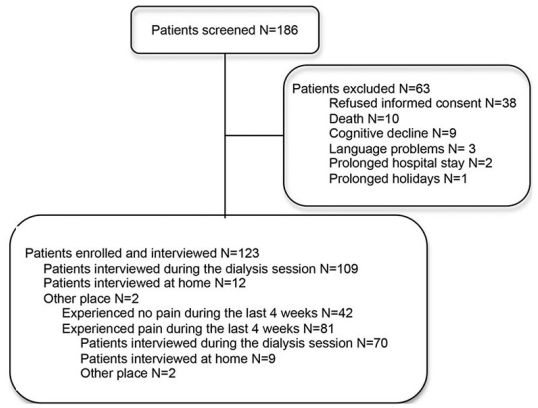

Figure 1

Number of patients screened and interviewed.

Statistical analyses

The statistical analyses were performed using SPSS (ver. 17; SPSS Inc., Chicago, Illinois, USA). Prevalence and severity of symptoms were described using proportions, means or medians, as appropriate. The one-sample Kolmogorov-Smirnov test was used to check for normal distribution of the data. Categorical data were compared using the chi-square or Fisher's exact test. Spearman's rho was used to compute univariate correlations. Multiple linear regression was used to study the multivariate relationship between pain and its predictors. Variables are expressed as mean ± standard deviation (SD), if not specified otherwise. The significance level was set to $\alpha = 0.05$, two-tailed.

Results

Demographics

Between September 2008 and March 2009, 123 consecutive patients were enrolled and 109 (88%) have been interviewed during dialysis (fig. 1). Population and dialysis characteristics are displayed in table 1 and are similar to those generally described for CKD patients. Hypertension

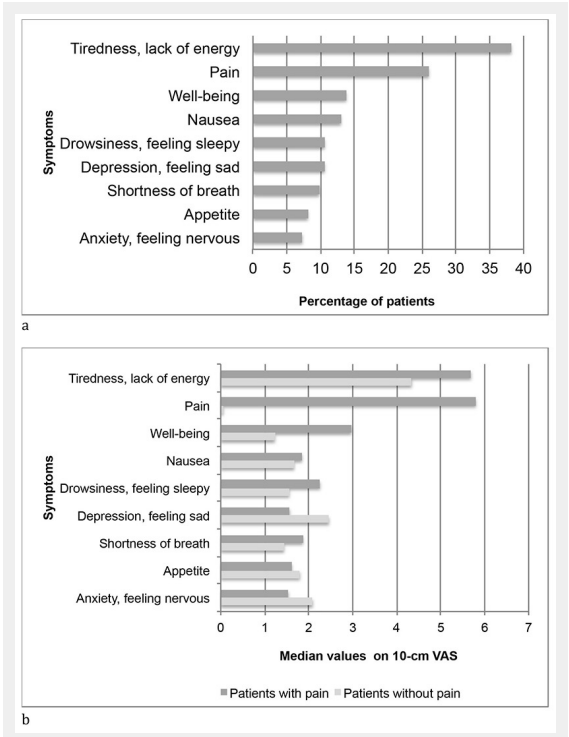

Figure 2

Outcome of ESAS: a. Percentage of patients with score >4 (n = 123). b. Median values of items on 10-cm VAS for patients with (n = 81) and without pain during the last 4 weeks (n = 39; missing 3). High values indicate high burden.

was the most frequent comorbidity. The mean time on dialysis was 3.5 years (range 1–22 years): 78% of the patients were on dialysis for 1–5 years, 11% for 5–10 years, 7% for less than 1 year and 4% for more than 10 years. The most recent laboratory Kt/V value (1.41 ± 0.27, range: 0.94–2.29, n = 99) and normalised protein catabolic rate (nPCR) value (1.13 ± 0.28, range: 0.67–1.73, n = 51) showed that dialysis was effective in all patients. Sixty-five percent of the patients had excellent acceptance of dialysis, 20% satisfactory acceptance and 13% bad acceptance, as judged by dialysis nursing staff.

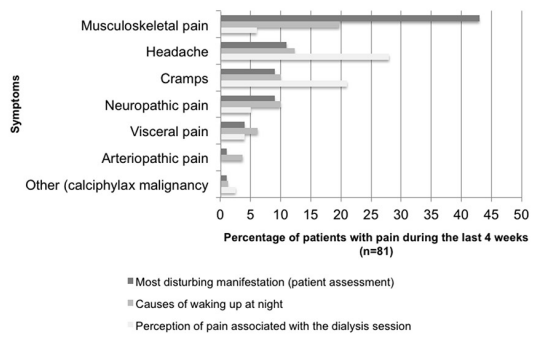

Figure 3

Important pain symptoms in different situations (n = 81).

Overall symptoms (ESAS)

In the whole population (n = 123), tiredness and pain were the symptoms most commonly perceived as a burden (ESAS score >4) (fig. 2), and were reported to be clinically relevant by the 81 patients complaining of pain during the previous 4 weeks (score >5). Median values for depression/feeling sad and anxiety/feeling nervous scored higher in patients without pain than in those with pain during the previous 4 weeks (fig. 2).

Concomitant symptoms

Asthenia and fatigue were the most common concomitant symptoms, being present in 54 (44%) of the patients. In addition, 25 (20%) said they suffered from sleep disturbance

Table 1: Population and dialysis characteristics, haematology parameters (N = 123).

Mean age (years; mean ± SD) (range)	71 ± 12.5 (36–90)	
Mean BMI (kg/m^2; mean ± SD) (range)	27 ± 5.5 (16–47.5)	
Gender: male/female (n and %)	75/48	61%/39%
Household situation (n and %): Living alone Living with others	 36 85	 29% 71%
Years of treatment (n and %): <1 1–5 5–10 >10	 9 96 13 5	 7% 78% 10% 5%
Modality of treatment (n and %): Haemodialysis Haemodiafiltration Not available	 69 50 4	 56% 41% 3%
Filters (n and %): High flux Low Flux Not available	 97 20 6	 79% 16% 5%
Comorbidities in >30% of the patients (n and %): Hypertension Coronary heart disease Diabetes mellitus Peripheral vascular disease Gastrointestinal and liver disease	 91 56 41 39 38	 74% 45% 33% 32% 31%
Haematology parameters	**Mean (range)**	**SD**
Haemoglobin (g/dl)	11.80 (8.5–15)	1.7
Haematocrit (%)	36 (26–49)	3.8
Ca^{++} (mmol/l)	2.21 (1.14–2.62)	0.2
$PO4^{--}$ (mmol/l)	1.5 (0.53–3.28)	0.5
$_{i}$PTH (pmol/l)	23 (1–127)	19.3
Albumin (g/l)	34.5 (20–45)	3.8
Ferritin (µg/l)	306 (11–1054)	220
PCR (mg/l)	14.5 (0.8–191)	24.7
Total cholesterol (mmol/l)	4.3 (1.9–7.4)	1.2
Triglycerides (mmol/l)	2.1 (0.4–8.0)	1.3
Dialyse-quality parameters	**Mean (range)**	**SD**
Kt/V (n = 112)	1.41 (0.94–2.29)	0.27
nPCR (n = 51)	1.13 (0.67–1.73)	0.28

Abbreviations: SD, standard deviation; BMI, body mass index; iPTH, intact parathyroid hormone; PCR, protein/creatinine ratio; nPCR, normalised protein catabolic rate.

and 21 (17%) reported constipation. Anxiety and depression were each present in 13 (10.5%) patients (table 2).

Factors correlated with pain

Univariate analyses showed that pain perceived during the previous 4 weeks was correlated with dyspnoea, asthenia/fatigue, loss of appetite, nausea/vomiting, constipation, anxiety and sleep disturbances. Only dyspnoea and fatigue were correlated with pain in the multivariate model. Pain perceived at the interview was correlated with asthenia/fatigue, loss of appetite, anxiety and sleep disturbances using the univariate model. Multivariate analyses did not show any correlation with concomitant symptoms. Other factors, such as Kt/V value, ferritin value, gender and acceptance of dialysis therapy were not correlated with pain during the last 4 weeks. However, recent Kt/V value (univariate model), female gender (univariate and multivariate model) and bad acceptance of dialysis therapy, as judged by the healthcare team (multivariate model) were correlated with pain at the interview. Ferritin values were not correlated to pain (table 3).

Population with pain during the previous 4 weeks (n = 81)

In our population, 81 (66%) of the 123 patients reported pain during the previous 4 weeks. Of these, 38 (47%) had experienced pain for 1–5 years and 23 (28%) for >5 years. Intense pain (VAS score 8–10) was reported by 49 (60.5%), moderate pain (VAS score 5–7) by 17 (21%), and mild pain (VAS score <4) by 17 (17.3%). At the time of the interview, 55 (68%) patients said they did not experience pain. Episodic pain was present in 63 (59%) patients and continuous pain in16 (12%); 26 (32%) patients had pain during the dialysis session and 11 (14%) during movement. Musculoskeletal pain was the most prevalent (52 patients, 64%), headache and cramps, respectively, were reported by 25 (31%) and 20 (25%) patients (table 4). Musculoskeletal pain was perceived as the most disturbing symptom and being the major cause of night awakening, whereas during the dialysis session headache and cramps predominated (fig. 3).

As analgesic therapy, the use of non-steroidal anti-inflammatory drugs (NSAIDs) or similar agents predominated (65 patients, 80%), whereas 13 (16%) patients were treated with weak opioids and 4 (5%) with strong opioids. Only 35 (43%) patients used laxatives (table 5). Ten (12%) patients received treatment specifically for their musculoskeletal pain.

When asked specifically, 29 (36%) patients said they woke up at night because of pain several times a week. In 16 patients the cause was musculoskeletal pain, in 10 headache, and cramps and neuropathic pain in 8 each (fig. 3). Changing position helped in 9 cases, movement in 8 and drug use in 5, 7 patients reported that they lacked any strategy for pain control in such a situation. Twenty-two (75%) patients said that they were being treated with nonopioid analgesics, 14 (48%) with laxatives, 6 (21%) with analgesics for neuropathic pain, 5 (17%) with opioids for moderate pain, 3 (10%) with opioids for severe pain, 3 (10%) with muscle relaxants.

Sixty-one (75%) patients reported that pain completely or partly limited their daily activities. Housekeeping was the activity most often limited, as indicated by 47 (58%) patients, followed by grocery shopping in 30 (38%) and cooking in 25 (31%). Only 12 (15%) felt that pain limited their own therapy.

Discussion and conclusions

The interviewed patients had chronic kidney disease (CKD) stage 5 and were on long-term dialysis. They experienced multiple and severe symptoms, which interfered with daily living.

The prevalence of pain in our population was similar to or larger than that observed in other studies conducted in the same population of haemodialysis patients [4, 5, 27].

Musculoskeletal pain prevailed in our cohort and was experienced as more bothersome than other pain types; this

Table 2: Patients reporting concomitant symptoms (N = 123).

		Number	%
Asthenia/fatigue	No	69	56.1%
	Yes	54	43.9%
Sleep disturbances	No	98	79.7%
	Yes	25	20.3%
Constipation	No	102	82.9%
	Yes	21	17.1%
Nausea/vomiting	No	105	85.4%
	Yes	18	14.6%
Loss of appetite	No	106	86.2%
	Yes	17	13.8%
Dyspnoea	No	107	87.0%
	Yes	16	13.0%
Anxiety	No	110	89.4%
	Yes	13	10.6%
Depression	No	110	89.4%
	Yes	13	10.6%
Nightmares	No	123	100.0%
	Yes	0	0.0%
Hallucinations	No	123	100.0%
	Yes	0	0.0%

was consistent with the perception of some patients that movement was a pain trigger.

Musculoskeletal pain is one of the leading causes of chronic health problems in people over 65 years of age. Studies suggest a high proportion of older adults suffering from musculoskeletal pain (65% to 80%) and back pain (36% to 40%) [28]. It is very difficult to conclude from our results if, and to what extent, dialysis influenced musculoskeletal pain in our population, because there are many factors implicated in the aetiopathology of bone pain in dialysed patients.

In our population, musculoskeletal pain was a leading cause of sleep disturbances and waking up at night, and it was treated with opioids in only a very few patients. Sleep disturbances include a variety of disorders in ESDR patients: difficulties in falling asleep and awakening, interrupted sleep, nightmares, restless legs syndrome, sleep apnoea syndrome and others [29]. The occurrence of sleep disturbances in our cohort is confirmed by other published data [2, 3]. The major aetiological factors for sleep disorders in the uraemic patient are still controversial. Pain is rarely identified as a trigger.

Poor sleep quality, with a prevalence of 49%, was observed in the haemodialysis patients included in the Dialysis Outcomes and Practice Patterns Study (DOPPS) population. It was independently associated with a higher degree of physical pain, higher medication use and mortality [23, 30, 31]. Diabetic haemodialysis patients also have an increased risk of insomnia [32], increased body pain and reduced quality of life [31].

Our population identified pain as an important factor related to frequent awakenings.

Patients identified the dialysis session itself as a trigger for headache and cramps. These painful syndromes are typical for CKD and are often dialysis-related, because of the disequilibrium of electrolytes that occurs during the dialysis session. Worsening of pain during haemodialysis is described but pathophysiologically-based treatments are matter of hypothesis [2, 3].

Table 3: Factors correlated with pain.

	Pain during previous 4 weeks (N = 123)				**Pain at the interview (N = 123)**			
	Univariate analysis		**Multivariate analysis**		**Univariate analysis**		**Multivariate analysis**	
Concomitant symptoms								
Dyspnoea	Pearson correlation	**0.402****	Model coefficient	**4.2****	Pearson correlation	0.099	Model coefficient	0.08
	p-value	*0.000*	*p-value*	*0.002*	*p-value*	*0.278*	*p-value*	*0.913*
Asthenia/fatigue	Pearson correlation	**0.404****	Model coefficient	**3.0****	Pearson correlation	**0.195***	Model coefficient	0.43
	p-value	*0.000*	*p-value*	*0.002*	*p-value*	*0.031*	*p-value*	*0.432*
Loss of appetite	Pearson correlation	**0.259****	Model coefficient	1.5	Pearson correlation	**0.178***	Model coefficient	0.98
	p-value	*0.004*	*p-value*	*0.226*	*p-value*	*0.049*	*p-value*	*0.18*
Nausea/vomiting	Pearson correlation	**0.181***	Model coefficient	0.6	Pearson correlation	0.072	Model coefficient	-0.73
	p-value	*0.045*	*p-value*	*0.600*	*p-value*	*0.429*	*p-value*	*0.284*
Constipation	Pearson correlation	**0.307****	Model coefficient	**2.5***	Pearson correlation	0.168	Model coefficient	0.65
	p-value	*0.001*	*p-value*	*0.032*	*p-value*	*0.064*	*p-value*	*0.344*
Anxiety	Pearson correlation	**0.264****	Model coefficient	-0.8	Pearson correlation	**0.256****	Model coefficient	1.4
	p-value	*0.003*	*p-value*	*0.573*	*p-value*	*0.004*	*p-value*	*0.105*
Depression	Pearson correlation	0.161	Model coefficient	-.1.7	Pearson correlation	0.101	Model coefficient	0.015
	p-value	*0.076*	*p-value*	*0.237*	*p-value*	*0.267*	*p-value*	*0.985*
Sleep disturbances	Pearson correlation	**0.400****	Model coefficient	1.9	Pearson correlation	**0.245****	Model coefficient	1.1
	p-value	*0.000*	*p-value*	*0.092*	*p-value*	*0.006*	*p-value*	*0.085*
Other factors								
Recent Kt/V value	Pearson correlation	0.094	Model coefficient	0.18	Pearson correlation	**0.242***	Model coefficient	0.74
	p-value	*0.326*	*p-value*	*0.909*	*p-value*	*0.01*	*p-value*	*0.424*
Recent ferritin value	Pearson correlation	-0.110	Model coefficient	0.002	Pearson correlation	-0.013	Model coefficient	0.0
	p-value	*0.231*	*p-value*	*0.335*	*p-value*	*0.89*	*p-value*	*0.853*
Female gender	Pearson correlation	0.015	Model coefficient	0.5	Pearson correlation	**0.253****	Model coefficient	**1.6****
	p-value	*0.868*	*p-value*	*0.562*	*p-value*	*0.005*	*p-value*	*0.003*
Acceptance of dialysis therapy	Pearson correlation	0.041	Model coefficient	0.045	Pearson correlation	-0.168	Model coefficient	**-0.17***
	p-value	*0.659*	*p-value*	*0.729*	*p-value*	*0.066*	*p-value*	*0.033**

** Correlation significant at p <0.01 level, 2 tailed
* Correlation significant at p <0.05 level, 2 tailed

In our population, 81% of the patients with pain recorded values of 8–10 in the VAS scale. The patients described the dialysis session asa pain trigger. Up to one-third of the patients describing other symptoms, such as nausea and vomiting, or dyspnoea, indicated VAS values higher than 5. This indicates a high level of global distress.

In the literature, the severity of symptoms in dialysis patients has been reported to be comparable to or even worse than in patients with CKD stage 5 managed without dialysis [2, 3]. On the other hand, the proportion of patients in our cohort with asthenia and fatigue, poor appetite, or dyspnoea was smaller than that of patients with stage 5 CKD managed without dialysis. In fact, previous studies report a prevalence of lack of energy and fatigue in as many as 75% of patients, poor appetite in 58% and dyspnoea in 49%, as compared with 58%, 19% and 19%, respectively, in our study population [2, 3].

Table 4: Pain duration, intensity, perception and localisation in the patients reporting pain during the 4 weeks before the interview (N = 81).

	N (%)*
Duration:	
<6 months	16 (20%)
6 months to 1 year	7 (9%)
1–5 years	38 (47%)
>5 years	23 (28%)
Intensity during the previous 4 weeks:	
Intense (VAS score 8–10)	49 (60.5%)
Moderate (VAS score 5–7)	17 (21%)
Mild (VAS score <4)	14 (17.3%)
No pain	0
Intensity at the time of interview:	
Intense (VAS score 8–10)	5 (6%)
Moderate (VAS score 5–7)	7 (8.5%)
Mild (VAS score <4)	13 (16%)
No pain	55 (68%)
Perception:	
Episodic pain	63 (59%)
Continuous pain	16 (12%
Localisation by the patient:	
Lower limbs	65 (80.5%)
Upper limbs	40 (50%)
Thorax	36 (44%)
Head	26 (32%)
Back, vertebral column, lumbar region	22 (27%)
Abdominal region	11 (13.5)
Chest	3 (3.5%)
Localisation by the physician:	
Musculoskeletal pain	52 (64%)
Headache	25 (31%)
Cramps	20 (25%)
Neuropathic pain	14 (17%)
Visceral pain	10 (12%)
Arteriopathic pain	7 (9%)
Other (calciphylaxis, malignancy)	2 (2%)

* Missing values have not been included in the totals; figures, therefore, may not always add up to 100.

Table 5: Pharmacotherapy (N = 81).

Pain specific pharmacotherapy:	**N**	**%**
Non-steroidal anti-inflammatory drugs or similar	65	80
Weak opioids	13	16
Strong opioids	4	5
Non-opioid topical analgesics	3	4
Drugs for neuropathic pain	9	11
Steroids	19	15
Antidepressants	8	10
Other pharmacotherapy:		
Laxatives	35	43
Other	18	21
Antiemetics	15	19
Anti-Parkinson treatment	3	4
Myorelaxants	2	3

The benefit of a high-quality dialysis session in terms of lower fatigue or symptom burden and pain related to the session itself should be balanced by corresponding pain treatment. Pain assessment and treatment during the dialysis sessions, and the assessment of overall symptoms by means of the ESAS, could help in developing early specific pain-relief protocols.

Data provide evidence that dialysis patients with chronic pain suffer more from insomnia and depression than those without pain, and that these symptoms are not adequately treated [33, 34]. In our study, 13% of the patients had significant levels of depression, as assessed using the ESAS. The size of our population does not allow further analysis, but it can be hypothesised that high levels of pain could be related with depression and affects daily living.

As pain therapy, opioids were prescribed to only 21% of our patients; nonopioid analgesics (mainly NSAIDs) were taken by 80% of the patients. A recent systematic review of the use of opioids in ESDR patients confirmed that the prevalence of opioid use is highly variable, ranging from 5% to 36% [35], suggesting a substantial under treatment of pain. Clear guidelines for pain management in dialysis patients are warranted to avoid under-prescription of analgesics, and also to consider their prescription in ESDR [12].

Improvement of sleep quality could lead to less fatigue, since in our study fatigue was not associated with haemoglobin levels. Management of sleep quality, however, requires adequate pain relief, which should focus primarily on musculoskeletal pain, as in our study it emerged as the most bothersome pain. Future pain management has also to consider the lack of correlation, as seen in our study, between hypertension and severity of pain, as well as hyperparathyroidism and musculoskeletal pain [27], although musculoskeletal pain was prevalent in our study.

The high burden of physical and psychological symptoms is known to be multifactorial, and in our study it was associated with impaired daily activity and a considerable impact on quality of life and independence [21].

With an estimated prevalence of 14% to 30%, major depression is the most common psychiatric problem in patients with stage 5 chronic kidney disease [36].

The dialysis patient's perception of symptom burden may be more important than objective clinical parameters in determining quality of life in this patient population, because quality of life is an important outcome in the treatment of end-stage renal disease [23].

The increasing number of patients with ESRD calls for the development of appropriate care models for these patients and their families, involving dialysis providers, doctors and nurses, and primary care and palliative care providers. A first step in the routine care in renal units could be a regular, comprehensive symptom assessment, especially in dialysis patients with advanced stages of CKD. In our study, ESAS has proved to be a simple, easily understandable tool to evaluate symptom burden in haemodialysis patients. Renal units should pay more attention to the K/DOQI Clinical Practice Guidelines, which recommend regular assessment of quality of life for all patients with CKD [18, 23]. This should also include the recognition and treatment of spiritual and emotional suffering in these patients.

Our study focused only on global symptom prevalence in a relatively small number of patients and does not allow firm correlations. The 4-week recall period might have biased the scoring of pain intensity and burden, as well as the questions on impact on daily life activities. The results rely on the patients' subjective perception. However, the outcome is in line with published literature and thus bias can be considered as minimal. Our observations provide further evidence of the need to include pain relief protocols in the treatment of dialysis patients, together with a comprehensive palliative care approach in our community.

Acknowledgement: The authors are grateful to the participating patients for giving us the opportunity to understand better their suffering, to Sistiana Nava-Santinelli and Silvia Walther (IOSI) for interviewing the patients, to Dr. med. Hans Neuenschwander (Palliative Care Service, Istituto Oncologico della Svizzera Italiana, Bellinzona, Switzerland) for his guidance during the study, to PD Dr. med. Michael Dickenmann (Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Switzerland) for his contribution during editing of the manuscript, to Mr. C. Limoni (Riva San Vitale, Switzerland) for reviewing the statistical analyses, to Liliane Petrini (Ph.D, Breganzona, Switzerland) for her help to finalizing the manuscript.

Funding / potential competing interests: The "Alfred und Erika Bär-Spycher Stiftung", Auf der Wacht 41, 4104 Oberwil BL, Switzerland, provided financial support for interviewing the patients, evaluating the data and using medical writing services by Dr. Liliane Petrini, PhD, for manuscript finalisation and submission. The "Alfred und Erika Bär-Spycher Stiftung" financial support is gratefully acknowledged. This was an investigator-initiated study. All authors declare that they have no conflicting relationships with companies or individuals concerning the information contained in this manuscript.

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Figures (large format)

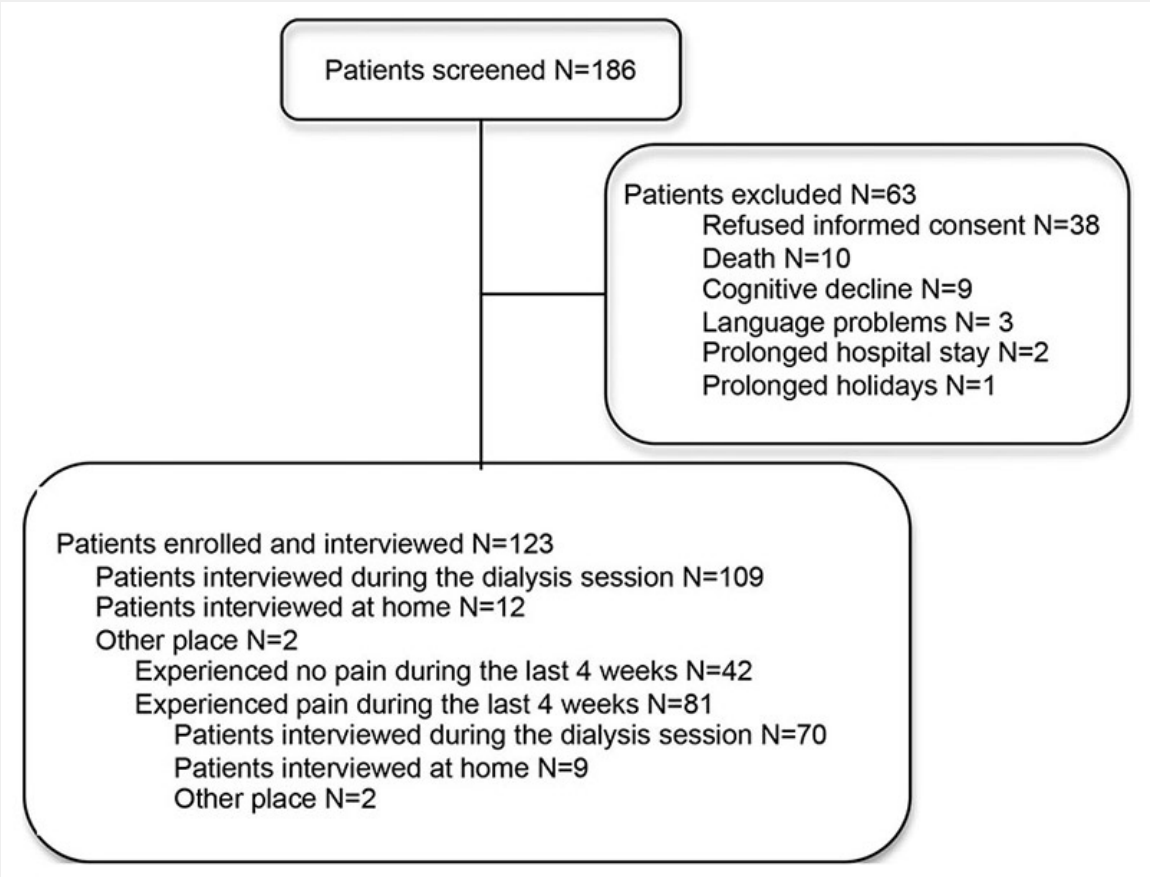
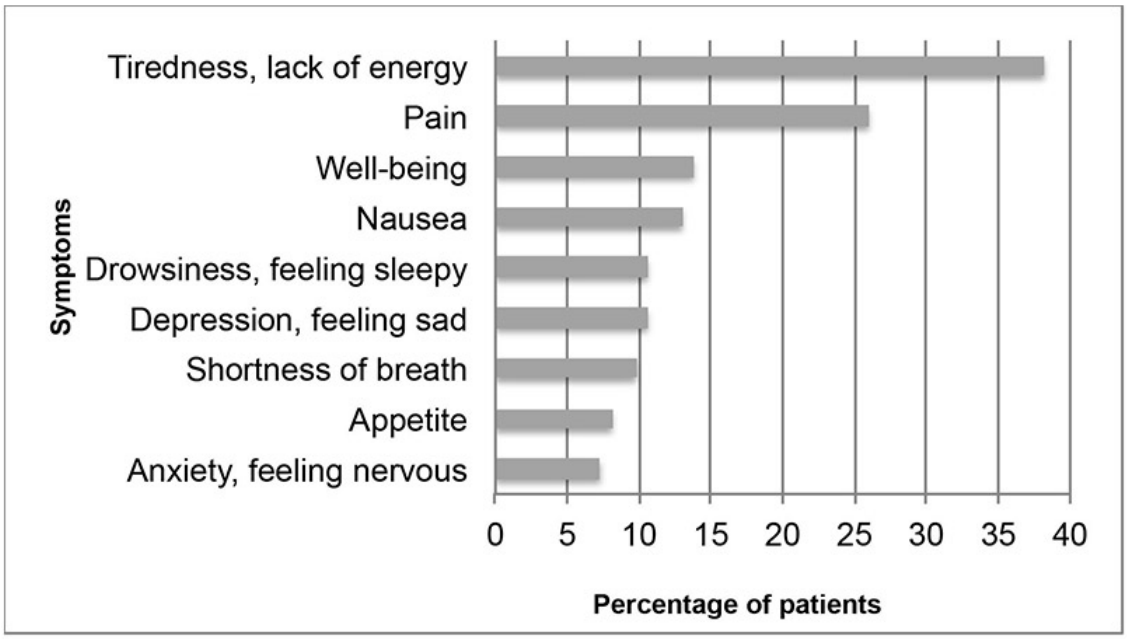


Figure 1

Number of patients screened and interviewed.



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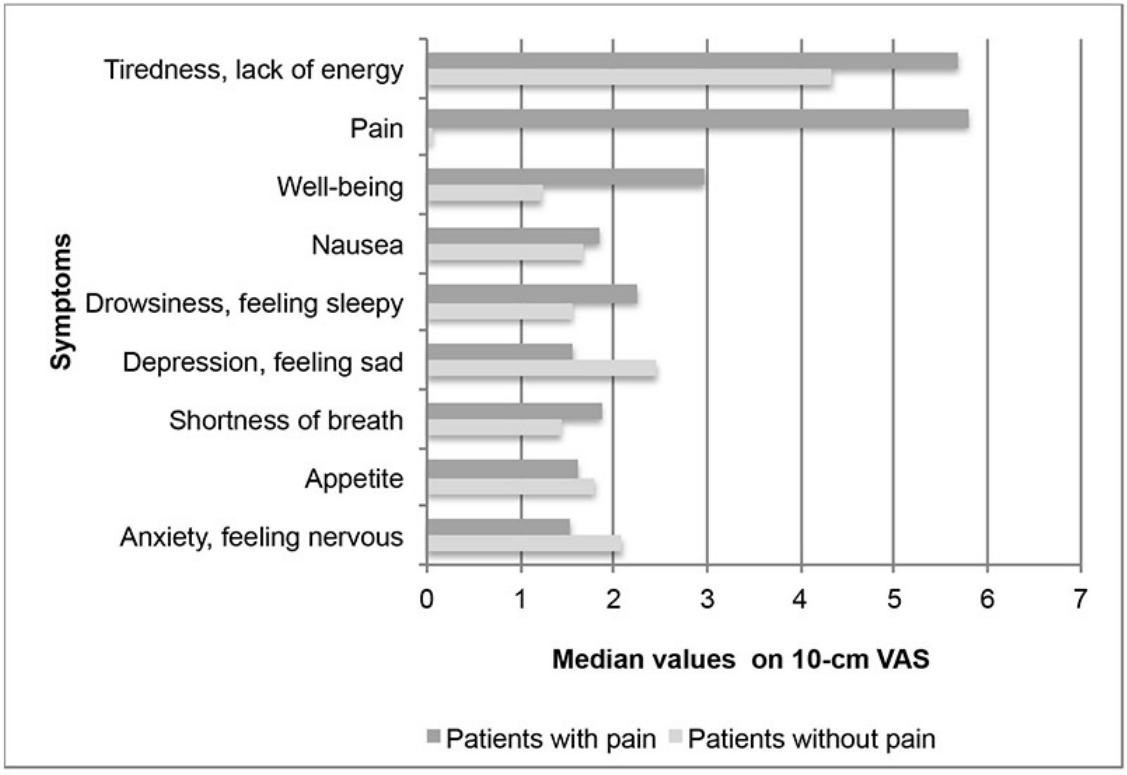

b

Figure 2

Outcome of ESAS: a. Percentage of patients with score >4 (n = 123). b. Median values of items on 10-cm VAS for patients with (n = 81) and without pain during the last 4 weeks (n = 39; missing 3). High values indicate high burden.

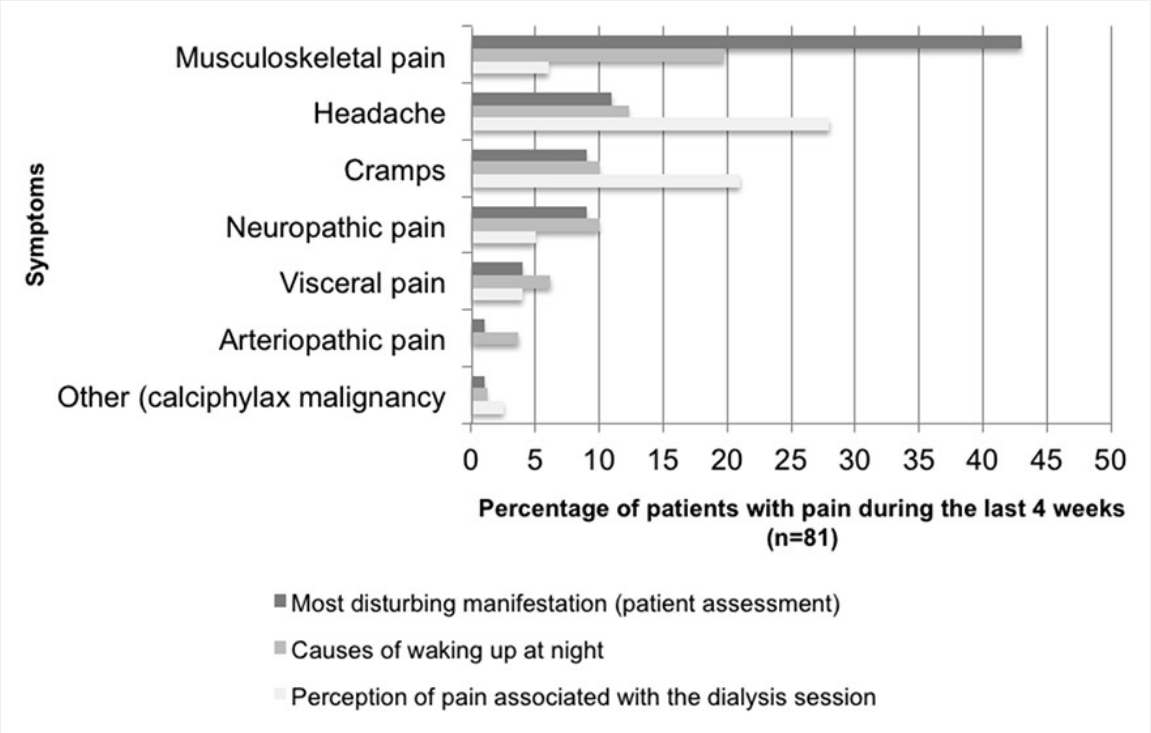

Figure 3

Important pain symptoms in different situations (n = 81).