NDT Perspectives

A systematic review regarding the association of illness perception and survival among end-stage renal disease patients

Mihaela Parfeni1,
Ionut Nistor2,3
and Adrian Covic1,2

Correspondence and offprint requests to: Ionut Nistor; E-mail: ionutni@yahoo.com

Keywords: dialysis, end-stage renal disease, illness perception, mental representation, survival

ABSTRACT

Background. End-stage renal disease (ESRD) patients have increased mortality and morbidity. According to Leventhal’s self-regulation model, these patients mentally develop illness representations and coping strategies in order to better understand their condition. Mental representations seem to be an important factor for clinical and psychosocial outcomes. We aimed to systematically review all available data regarding the association between illness perception and survival/mortality among ESRD patients receiving dialysis treatment.

Methods. This is a systematic review of prospective observational studies, evaluating illness perception and its association with survival/mortality in ESRD dialysis stage patients. We searched CENTRAL in the Cochrane Library until August 2012, MEDLINE from 1950, EMBASE from 1980, PsychINFO from 1967 and additional sources to identify all records evaluating illness perception and clinical outcomes in this population. Two authors assessed potential citations for eligibility and extracted all data. The studied intervention was the application of the most commonly used questionnaires for assessing illness perception. The main outcomes were survival and mortality.

Results. We identified five studies evaluating the relationship between illness perception and survival/mortality in ESRD patients receiving dialysis treatment. All included studies were prospective observational ones. Four studies showed that a negative perception of illness is associated with increased risk of death and one study failed to find any association between illness perception and mortality. This is the first systematic search that analysed the existing data showing an association between illness representation and survival/mortality among these patients. The main limitation of this review includes the design of the included studies (prospective observational studies without a non-exposed control group).

Conclusions. This study implies that patient’s outcome may be improved by changes in illness perception and designing appropriate interventions. We conclude that these findings constitute an important indication for future research in this field (high-quality randomized trials) and for future implementation of effective interventions that could improve this patients’ outcome.

INTRODUCTION

End-stage renal disease (ESRD) is a worldwide health problem associated with increased mortality and mortality; the mean expected remaining life span for patients after initiation of dialysis treatment is 10.7 years for patients between the age 40–44 years and 5.6 years for patients between the age 60–64 years, according to the ERA-EDTA Registry Annual Report 2010 [1]. In addition, ESRD also implies a major life disturbance (possibly more important than in any other chronic illness), mainly due to severe metabolic and cardiovascular complications, total dependency of dialysis machines with stringent dialysis schedules—a unique combination with a major social, familial and professional impact [2].

When individuals develop a physical disease, they tend to generate a specific pattern of beliefs and opinions that have the main role of helping them to understand their illness. More specifically, this ‘mental representation’ of the disease is
considered to be the ‘ground stone’ in the beginning of any cognitive management of the disease, in parallel with the initiation of coping strategies (see Figure 1). Individual understanding of events and their mental representation as a health threat determine the way in which a patient will respond to it. At the same time, patients develop ‘implicit theories of illness’ (illness schemata) that will further regulate the response to their health behaviour, according to the common sense model of self-regulation (CSM)—Leventhal’s approach [3]. The association between illness perception and survival/mortality was reported in non-renal chronic diseases. A study performed in patients with myocardial infarction indicated that illness perception questionnaire (IPQ) scores were predictive of the occurrence of any complication (for one unit increase in the IPQ score, the odds to experience a complication increased by 5.1%; overall, 75.5% of all complications were predicted correctly) [4].

Our group [5] previously described, for the first time, in a well-established haemodialysis (HD) population without significant confounding comorbidities, the cognitive representation of illness and the relationship between illness perception and perceived quality of life (QoL). The results of the study showed that patients understood their illness and its chronic course, considered that their own actions could influence the disease and concluded that illness representation could be interpreted as a powerful predictor of QoL in ESRD patients [5].

However, there is no systematic review of the existing contradictory evidence describing an association between illness perception and survival/mortality among ESRD patients. Therefore, it is still unclear whether there is any relationship between illness representation and different outcomes in ESRD patients. The purpose of this systematic review was to consider the role of illness perception beliefs in relation to survival/mortality among ESRD patients.

FIGURE 1. Mental representation of a health threat.

MATERIALS AND METHODS

Inclusion/exclusion criteria

The literature was reviewed for all randomized controlled trials, cohort studies (with or without comparison group), comparative and case–control studies evaluating the relationship between illness perception as described by the authors (any pre-specified tools was included) and survival/mortality. We included patients with pre-dialysis chronic kidney disease (CKD) and ESRD (children, adults or elderly patients) on HD or continuous ambulatory peritoneal dialysis (CAPD).

The search included the following illness representation measurement tools: the IPQ, the revised illness perception questionnaire (R-IPQ), the brief illness perception questionnaire (B-IPQ) and the illness effects questionnaires (IEQ), with or without other types of psychological or psychosocial measurement tools, with or without pharmacological and clinical interventions. Each questionnaire that was used is described in detail in Table 1.

Search strategy

The search outcome was overall mortality as reported by the authors, including all deaths from any cause at any time point. The search strategies we used to retrieve studies from the bibliographic databases combined medical subject headings and text words for CKD and ESRD limiting to studies conducted in humans. We did not apply a methodological filter nor did we impose any restriction on language. The search strategies are detailed in Supplementary data, Appendix 1. To identify studies for inclusion in this review, in August 2012, we searched CENTRAL in the Cochrane Library, MEDLINE from 1950, EMBASE from 1980, PsychINFO from
1967, reference lists of nephrology textbooks, review articles and relevant studies.

We checked the reference lists of all potentially eligible studies as full reports to identify any further studies not retrieved by electronic search. We also obtained full reports of review articles retrieved by the search and checked these for other relevant citations. We did not find any other records through searching additional sources or any unpublished data.

### Assessment of the methodological quality

Two authors assessed the quality of the included studies. The Newcastle–Ottawa scale (NOS) for assessing the quality of non-randomized studies was used. The NOS scale includes three sections: selection criteria, comparability and outcome, each one divided into multiple subscales. A study can be awarded a maximum of one star for each numbered item within the selection and outcome categories and a maximum of two stars can be given for comparability [6]. A description of quality assessment of the included studies is provided in Supplementary data, Table S1. Two authors extracted data from the studies, using a data extraction form. Each author double-checked data extraction and data entry independently and any discrepancies between the authors were resolved by discussion.

#### RESULTS

**Study selection process**

We identified a total number of 250 studies of which 19 were removed (duplicates) and 132 were considered not...
relevant based on the title and abstract. We identified 99 potentially relevant citations that were full-text reviewed. Ninety-three were further excluded for the following reasons:

- not the right intervention ($n = 31$): studies conducted in ESRD patients that measured the QoL ($n = 19$), depression ($n = 3$), social support ($n = 2$), other ($n = 7$);
- not the right outcome: studies conducted in ESRD population that used IPQ, B-IPQ, IPQ-R, IEQ but did not assess their relationship with survival/mortality ($n = 46$);
- improper study design ($n = 17$): review, editorial, comment letter, protocol validation studies.

Overall, we finally included only five studies (including two studies that analysed different subgroups from the same population) (Figure 2).

There was no single study describing any association between illness perception and survival/mortality in CKD pre-dialysis stages. From the five identified studies in ESRD, only two included both HD and PD as treatment options [7, 8]; the other three included only HD patients [9–11]. On average, the number of participants in each study was small, ranging between 57 and 295 patients (see Table 2). Three studies used as measurement tool IEQ [7, 9, 10] and the other two used IPQ-R [8, 11].

Characteristics of the analysed cohorts in four of the five studies were generally satisfactory [8–11]. All of the studies mentioned inclusion-exclusion criteria, but only three stated them explicitly [9–11]. Only one study clearly described the selection process [11]. Only one study stated as inclusion criterion fluency in verbal and written English language [11]. Only one study excluded patients who had a psychiatric diagnosis of psychosis and those who scored <23 points on a mini-mental examination [9].

Of the five selected studies, only four detailed other comorbidities [8–11], and no study listed any chronic medication.

One study detailed the duration of the dialysis procedure, the type of dialyser, the dialysis solution used and the dialysis prescription [11]. One study detailed the duration of the dialysis treatment, type of dialyser and compliance to treatment [9]. Two studies stated the duration of the dialysis treatment [8, 10].

In general, the studies showed some problems of selection bias: the majority used the same population, but no study reported a non-exposed cohort; all ascertainment of exposure was drawn from secure clinical records; no study could demonstrate the absence of outcome of interest at the start of study (in the case of mortality studies, outcome of interest is still the presence of a disease/incident, rather than death). Since many prognostic factors can themselves lead to mortality, adjustment for confounding factors is a relevant quality indicator. With the exception of one study where we could not find any adjustments [7], all of the other studies stated the adjustment for the most important risk factors. Ascertainment of outcome is not associated with a major bias in relation to the assessment of mortality, because mortality is often ascertained through reference to secure records or by record linkage. Losses to follow-up might represent a problem which appears to be minor for mortality studies, being ascertained through record linkage with mortality registry usually providing fairly complete follow-up or by secure data records. One study [11] reported the amount of losses to follow-up, so in our analysis there is a minor risk of bias in this category.

**Data on outcomes**

The first correlation between illness perception and mortality was reported by Peterson et al. [7] who conducted a prospective study, evaluating 57 patients with ESRD (43 treated

---

**FIGURE 2.** Selection process for inclusion of studies in the review.

M. Parfeni et al.
### Table 2. Characteristics of the included studies

<table>
<thead>
<tr>
<th>Study (reference)</th>
<th>Type of study</th>
<th>n</th>
<th>Age (mean) (years)</th>
<th>Gender</th>
<th>Ethnicity</th>
<th>RRT</th>
<th>Dialysis vintage (mean)</th>
<th>Follow-up</th>
<th>Associated comorbidities</th>
<th>Applied measure</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>van Dijk et al. [8]</td>
<td>Prospective, observational</td>
<td>182</td>
<td>67.3 ± 11.7</td>
<td>113 M69 F</td>
<td>Caucasian</td>
<td>139 HD; 43 PD</td>
<td>3.5 ± 2.3 year</td>
<td>3.5 year (average)</td>
<td>(i) Davies comorbidity score (none-67%, medium-31.3%, high-1.6%) (ii) primary cause of renal failure (diabetes mellitus-11.5%, glomerulonephritis-6.6%, renal vascular disease-13.7%, other cause-68.1%)</td>
<td>IPQ-R</td>
<td>Mortality rates were higher among patients who perceived their treatment as being less effective in regulating ESRD (P = 0.028)</td>
</tr>
<tr>
<td>Chilcot et al. [11]</td>
<td>Prospective observational</td>
<td>223</td>
<td>59.2 ± 16</td>
<td>147 M76 F</td>
<td>White</td>
<td>HD</td>
<td>1.46 ± 4.4 years</td>
<td>1.32 years (median)</td>
<td>extra-renal comorbidity-semi-quantitative method: none (0)-39.9%, medium (1–2)-29.1 high (3+)–30.9%</td>
<td>IPQ-R</td>
<td>Negative perception of treatment control was significantly associated with mortality (P = 0.03)</td>
</tr>
<tr>
<td>Peterson et al. [7]</td>
<td>Prospective observational</td>
<td>57</td>
<td>51.5 ± 17.9</td>
<td>30 M27 F</td>
<td>NS</td>
<td>HD; 14 CAPD</td>
<td>4 years</td>
<td>2 years – assessed through a severity coefficient</td>
<td>IEQ</td>
<td>Perception of illness was not significantly related to mortality (at one year follow-up IEQ did not significantly differ between the survivors and non-survivors groups; P = 0.26, results sustained at two year follow-up; P = 0.15)</td>
<td></td>
</tr>
<tr>
<td>Kimmel et al. [9]</td>
<td>Prospective observational</td>
<td>295</td>
<td>54.6 ± 14.1</td>
<td>209 M86 F</td>
<td>African-American</td>
<td>HD</td>
<td>4.71 ± 4.32 years</td>
<td>2.2 ± 1.06 years</td>
<td>(i) Cardiovascular and cerebrovascular disease (NS) (ii) Diabetes mellitus; (NS) (iii) Collagen vascular disease (NS) (iv) Malignancy (NS) (v) Type of renal (vi) Disease (NS)</td>
<td>IEQ</td>
<td>An increased patient perception of disruptive effects of illness was associated with a 23% increase in relative mortality risk.</td>
</tr>
<tr>
<td>Kimmel et al. [10]</td>
<td>Prospective observational</td>
<td>174</td>
<td>54 ± 13.8</td>
<td>134 M40 F</td>
<td>African-American</td>
<td>HD</td>
<td>2.38 ± 3.86 year</td>
<td>2.68 ± 0.95 years</td>
<td>– Diabetes Mellitus (44.3%)</td>
<td>IEQ</td>
<td>IEQ was found to be a successful parameter of predicting mortality (P = 0.03)</td>
</tr>
</tbody>
</table>

n, total number of patients included in the study; RRT, renal replacement therapy; M, male; F, female; NS, not stated; IPQ, illness perception questionnaire; IPQ-R, revised illness perception questionnaire; IEQ, illness effects questionnaire; ESRD, end-stage renal disease.
with HD and 14 with CAPD). The following measurement tools were used: IEQ, the beck depression inventory (BDI) and a cognitive item subset of the BDI—cognitive depression index (CDI). All patients were interviewed initially, at 1 and then at 2 years. Initially, the mean IEQ score (60.5 ± 27.5) suggested a negative perception of illness in the analysed population. At baseline, IEQ did not correlate with age or severity of ESRD coefficient, but correlated with CDI [7]. At 1-year follow-up, 10 patients had died, 8 treated with HD and 2 treated with CAPD (the death rates for the CAPD patients and HD patients were 14.3 and 18.6%). There was no significant difference in the baseline IEQ score of the non-survivors group (69.4 ± 23.6) and the baseline IEQ score of the survivors group (58.6 ± 28.1) [7]. At 2-year follow-up, a total of 21 patients died and 36 survived (the death rates for the CAPD patients and HD patients were 16.7 and 25.5%). Again, there was no significant difference in the baseline IEQ score for the non-survivors group (69.4 ± 23.6) and the baseline IEQ score of the survivors group (58.6 ± 28.1) [7] (see Table 2).

The authors concluded that although perception of illness was found to be an important determinant of cognitive depression, there was no data supporting its association with mortality. One limitation of this study is the small number of included patients that prevented the use of discriminant analysis and multivariable hazards analysis [7].

Van Dijk et al. [8] aimed to explore, in a cohort of 182 patients treated with HD and PD, nested within the Netherlands Cooperative Study on the Adequacy of Dialysis, the association between illness perception and mortality. Illness severity was assessed by measuring the levels of serum albumin, comorbidity and primary kidney disease. Each dimension of illness perception was measured using the IPQ-R. After an average follow-up of 3.5 years, 61 patients died (33.5%), the principal cause being cardiovascular disease. There was one dimension of the IPQ-R (perceived less effective treatment effects) that correlated with higher mortality rates and this remained statistically valid even after adjustment for clinical and socio-demographic variables. This is the first study to demonstrate that the patient’s illness perception regarding treatment control is associated with survival. One limitation of this study is in the patient population dialysis vintage: some patients had just started dialysis treatment, whereas others had survived for many years on dialysis already. A second limitation is the use of only primary kidney disease, comorbidities and serum albumin as indicators of illness severity, without conducting an adjustment for a wider range of other clinical parameters that indicate illness severity [8].

A recent study by Chilcot et al. [11] conducted in 223 patients treated with HD, from the renal service of the East and North Hertfordshire NHS Trust, assessed the perception of illness using IPQ-R and depression symptoms were measured using BDI questionnaires. After a median follow-up period of 15.9 months, 49 deaths were recorded. Treatment control dimension was significantly associated with mortality (a one point increase in treatment control perception—meaning a stronger sense of control—was associated with an 11% reduction in the hazard of death) after controlling for depression scores, independent predictors of survival (age, serum albumin levels, haemoglobin levels, comorbidity score, CRP, KPS < 70 and Kt/V) and dialysis vintage. One limitation of the study is represented by all-cause mortality used as an endpoint, without performing a discriminatory analysis on different types of deaths, preventing, in this way, the association between illness perception and particular cause of death (such as a possible occurrence of events due to non-adherence). A second limitation is represented by the lack of data collection regarding the measurement of non-adherence (phosphate levels, interdialytic weight gain and dialysis attendance), preventing the evaluation of hypothesized mediators between treatment control perception and survival. Also, important predictors of survival (blood pressure and medication) were not collected and controlled for in the survival analysis. The population was restricted to predominant white English-speaking patients [11].

In a study published in 1998, Kimmel et al. [9] aimed at determining the contribution of compliance and psychosocial factors to patient survival. A total of 295 patients treated with HD were included with a mean follow-up of 26.4 months. The exclusion criteria were: HIV-infected patients, those with documented psychosis and those who scored <23 on a mini-mental status examination. The administered questionnaires measured psychosocial variables—BDI and CDI, social support—the multidimensional scale of perceived social support, well-being—IEQ and the satisfaction with life scale and behavioural compliance. Comorbidities, nutritional and dialysis parameters were also measured. The study demonstrated that an improved illness perception of the effects of illness and increased behavioural compliance were significantly associated with decreased relative mortality risk. A 1 SD increase in IEQ scores (denoting an increased patient perception of disruptive effects of illness) was associated with a 23% increase in mortality risk, after controlling for age, severity of comorbid illness, level of serum albumin concentration and type of dialyser (P = 0.05). The limitation of the study is represented by the relatively small sample size, primarily comprised of African-American males [9].

In a later prospective study, conducted on the same population reported previously [9], Kimmel et al. [10] demonstrated that in a subset composed of 174 ESRD patients involved in a dyadic relationship for >6 months (40 women and 134 men) a lower IEQ score (indicating decreased levels of perceived life disruption from illness) correlated with decreased mortality risk. IEQ was found to be a successful predictor of mortality (RR = 1.37; CI = 1.02, 1.83; P = 0.03) [8]. The most important limitation of this study is a selection bias: the included population is just a subgroup analysis performed on patients in a relationship [9, 10].

**DISCUSSION**

From the five included studies in this systematic review, four of them showed that a negative perception of illness is associated with increased risk of death [8–11]. Only one study failed to find any association between illness perception and
mortality [7]. Two studies found the same dimension (negative perception of treatment control) of the IPQ-R to be associated with mortality [8, 11]. One study showed that a high perception of the disruptive effects of illness was predictive of increased mortality risk [9]. The last positive study did not state the specific attribute of illness representation that was found to be a predictor of mortality [10]. No study reported correlations between survival/mortality and more than one dimension of illness perception.

The results of these studies imply that a negative perception of several domains of illness representation is associated with increased risk of mortality among ESRD patients and that a positive perception of illness predicts better survival. However, our evaluation, using the NOS scale, also showed a mediocre quality of the existing studies (no study registered a maximum score). All of the five included studies are prospective observational and no single study reported an exposed cohort. The lowest NOS score was recorded by the first investigation that analysed the association of illness perception with survival/mortality in ESRD patients [7]. This only study found no significant association between illness perception and outcome—possible explanations for this could be the small study population (the smallest sample from all included studies) and, furthermore, the absence of adjustments for demographic characteristics and comorbidities in a multivariable hazard analysis [7].

The findings from the present systematic review are consistent with previous data from similar studies performed on non-renal chronic diseases (diabetes mellitus—Lawson et al. [12], Paschalis et al. [13]; cardiovascular disease—Ross et al. [14]; cardiac surgery—Jürgens et al. [15]; COPD—Kaptein et al. [16]; asthma—Kaptein et al. [16]; rheumatoid arthritis—Graves et al. [18]; Huntington’s disease—Kaptein et al. [19]) that also demonstrated an association between illness perception and decreased QoL, depression, non-adherence to treatment and worsen clinical outcomes [12–19].

In renal patients, a recent review by Chilcot et al. (including 11 studies performed in CKD patients) showed that several domains of the IPQ were associated with higher depression symptoms and noncompliance to treatment. The review also included two studies reporting that a lower perception of treatment control was a predictor of survival in ESRD patients [20]. In addition, another study, not included in this review due to the absence of mortality analysis, specifically aimed at determining if illness perception dimensions are a predictor of treatment adherence in HD patients failed to observe a positive connection with clinical outcomes [21].

In the absence of high-quality data from experimental studies or randomized trials in this area, observational studies pose the question whether patients’ outcome can indeed be improved by changes in illness perception and therefore by designing appropriate interventions. Non-renal literature data supports the hypothesis that the five cognitive domains of CSM of self-regulation should be integrated in a dynamic control system which will include output expectations and monitoring of the changes between the current status and desired endpoints [22]. The ‘bottom-up’ approach tries to achieve a view of the disease as a chronic condition requiring constant self-regulation and the use of objective monitoring devices (method used previously for diabetes—Horne et al. 2007) [22]. The ‘top-down’ approach offers patients a conceptual framework for the disease, so they can recognize that their illness is chronic and treatable, realizing its presence even when they are asymptomatic; at the same time it provides a model to correctly interpret bottom-up inputs generated by their actions (method previously used for asthma—Wagner et al. 1998) [22]. It is our belief that these two approaches could be implemented in the psychosocial management of CKD, thereby improving patients’ outcome.

The limitations of this systematic review are represented by the types of studies included (only observational prospective investigations, composed of small cohorts without any control group), the use of different measurement tools in each study, a lack of correlation between mortality and all of the existing domains of the IPQ. Nevertheless, to our knowledge, this article accounts for the first systematic search that considered the association between illness perception and survival/mortality among ESRD patients.

Overall, this review suggests that cognitive and emotional representations of illness play an important role in these patients’ outcome. We also consider that the described findings constitute an important indication for future research in this field and for future implementation of effective interventions.

SUPPLEMENTARY DATA
Supplementary data are available online at http://ndt.oxfordjournals.org.

AUTHORS’ CONTRIBUTION
M.P., I.N. and A.C researched, wrote and revised the manuscript.

CONFLICT OF INTEREST STATEMENT
M.P., I.N. and A.C have no relevant disclosures. They have no financial relationship or conflict of interest to disclose and take full responsibility for the data analysis and interpretation. Also, the results presented in this paper have not been published previously in whole or part, except in abstract format [23].

REFERENCES
27. Greenberg GD, Peterson RA. The Illness Effects Questionnaire—Multi-Perspective

Received for publication: 4.3.2013; Accepted in revised form: 5.4.2013