ORIGINAL RESEARCH

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Conservative management and health-related quality of life in end-stage renal disease: a systematic review

Abstract

Purpose: Few studies have addressed health-related quality of life (QoL) in patients who chose conservative management over dialysis. This systematic review aims to better define the role of conservative management in improving health-related QoL in patients with end-stage renal disease (ESRD).

Methods: Medline, Cochrane and EMBASE were searched for prospective or retrospective studies published until June 30, 2016, that examined QoL of ESRD patients. The primary outcome was health-related QoL.

Results: Four studies were included (405 patients received dialysis and 332 received conservative management). Two studies that used the Short Form-36 Survey (SF-36) showed that the dialysis group had higher physical component scores, but the conservative management group had similar, or better, mental component scores at the end of intervention. Another study using the SF-36 showed that the physical and mental component scores of the dialysis group did not significantly change after intervention. In the conservative management group, the physical component scores did not change, but the mental component scores increased significantly over time (0.12 ± 0.32 , $p < 0.05$). One study, which used the Kidney Disease Quality of Life-Short Form (KD QoL-SF), found no change after intervention in either physical or mental component scores in the dialysis group; however, the physical component score declined ($p = 0.047$) and the mental component score increased ($p = 0.033$) in the conservative management group.

Conclusion: Although there are only a limited number of published articles, ESRD patients who receive conservative management may have improved mental health-related QoL when compared with those who receive dialysis.

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Patients with end-stage renal disease (ESRD) can experience a significant symptom burden and complex comorbidities. The symptoms associated with ESRD are variable, and include nausea and vomiting, anorexia, insomnia, anxiety, depression and lethargy. These symptoms may be present for months, along with decreasing performance status. To prolong their lives, ESRD patients require renal replacement therapy (RRT), which can include kidney transplantation and dialysis. Due to limited donor availability in Asian countries, most ESRD patients have to rely on dialysis, either hemodialysis (HD) or peritoneal dialysis (PD). Dialysis patients are also confronted with different symptom burdens; while some uremic symptoms can be relieved by dialysis, the overall symptom burden remains high [1-4]. Thus, the choice between receiving dialysis to the end-of-life vs. conservative management can be a difficult decision for ESRD patients.

Palliative care is an approach to treating patients that can improve the health-related quality of life (QoL) of patients and their families facing life-threatening illness, such as ESRD, through the prevention and relief of suffering [5]. This suffering may include social, psychological, cultural and spiritual dimensions [6]. Suffering occurs when a person's social role, his relationship within the family, or what he values in his life is threatened [7]. Relief of suffering is accomplished by means of early identification and treatment of pain and other physical, psychosocial and spiritual problems [8]. The critical issues that should be discussed when patients are contemplating receiving dialysis include "Does the prolongation of life achieved by dialysis extend suffering?" and "Is there a reasonable probability of healing with an acceptable health-related QoL?" [1].

Research has shown that patients receiving dialysis may prioritize health-related QoL over survival time, partly due to the constraints that dialysis imposes [9]. In addition, dialysis may not provide a clear benefit over non-dialysis regarding survival and health-related QoL, especially in the presence of extensive comorbidities [10]. Advance care planning is an important process for those who choose not to continue dialysis. Introducing palliative care at an early stage for those patients who have chosen not to have dialysis can result in better symptom control, and can help ease the passage to end-of-life care [5].

When there is no residual renal function, patients who withdraw from dialysis have a very short survival time (average, 8-10 days; range, 1-46 days) [11]. Being in their preferred place of care at the end of life is very important for many ESRD patients. Research has shown that in elderly patients with significant comorbidities, the comorbidities should be one of

the main considerations when advising elderly patients on the choice for or against dialysis [12]; whereas, this may not be the case for an individual with no comorbidities or rapidly deteriorating renal function. Health-related QoL is a significant factor in this decision-making process [2,13]; however, only a few studies have addressed health-related QoL in patients who chose conservative management over dialysis [14-20].

This systematic review aimed to compare health-related QoL among patients with chronic kidney disease (CKD) who were currently receiving either dialysis or conservative management.

Materials and Methods

Selection criteria

Prospective and retrospective studies of patients with ESRD (i.e., renal failure or kidney failure) were included in the analysis. Non-English publications were excluded. Each included study included data from one group that received dialysis and one group that received palliative/hospice care/conservative care (non-dialysis). The primary outcome measure was health-related QoL. Any study that did not evaluate ESRD patients, evaluated only one type of intervention (no comparison), or had no health-related QoL measurement as its outcome was excluded.

Search Strategy

Databases searched included Medline, the Cochrane Library and EMBASE. Databases were searched up to June 30, 2016. Reference lists of relevant studies were hand-searched by two independent reviewers who then identified the studies according to the search strategy. Keywords used for the search included renal replacement therapy, RRT, palliative care, conservative management, chronic kidney disease, chronic kidney failure and ESRD.

Study and data extraction

Studies were identified by two independent reviewers (THB and CCT) using the same search strategy. When there was uncertainty regarding study eligibility, a third reviewer (CRE) was consulted and a consensus was reached among all three reviewers.

The following data were extracted from studies that met the inclusion criteria: the name of the first author, year of publication, type of study, type of patient, type of intervention, glomerular filtration rate, Karnofsky performance score (KPS),

hospital anxiety and depression scale (HADS), satisfaction with life scale (SWLS), Charlson comorbidity index (CCI), median survival, survival rate, health-related QoL and level of depression.

Outcome measures and quality assessment

The primary outcome measure was health-related QoL. Three of four studies [14, 15, 16], reported health-related QoL using the Short Form-36 Survey (SF-36), and the fourth study measured health-related QoL using the Kidney Disease Quality of Life-Short Form (KD QoL-SF) (version 1.2) [21]. SF-36 measured physical components (physical function (PF), role limitation due to physical health (RP), bodily pain (BP), general health (GH), vitality (VT)) and mental components (social functioning (SF), role limitation due to emotional problem (RE), and mental health (MH)). KD QoL-SF also examines physical and mental components.

The quality of included studies was assessed using the Newcastle-Ottawa Scale (NOS). NOS was developed to assess the quality of nonrandomized studies using a system by which a study is judged on three broad perspectives: the selection of the study groups, the comparability of the groups and the ascertainment of either the exposure or outcome of interest for case-control or cohort studies, respectively [22]. Using this scale, studies were scored across three categories: selection of study groups (four questions), comparability of study groups (two questions) and ascertainment of the outcome of interest (three questions). All questions have a score of one point, except for comparability of study groups, for which separate points are awarded for controlling for age and/or sex (maximum, two points). NOS assigns up to a maximum of nine points for the least risk of bias.

Results

Study characteristics and clinical outcomes

Of the initial 301 records identified through the database searches, 12 studies evaluated health-related QoL in ESRD patients receiving either RRT or conservative care. Once the full text of each of the 12 studies was reviewed, eight studies were excluded for the following reasons: (1) no health-related QoL information between the two groups [23, 24]; (2) no conservative management group (control group) [17, 25, 26]; and (3) no quantitative outcome of interest [11, 12, 27]. A flow chart outlining the study selection is shown in Figure 1.

The characteristics of the four studies included in the analysis, including patient demographic data, study type, stage of CKD and type of intervention, are summarized in Table 1.

There were two prospective longitudinal studies [14, 21], one prospective cross-sectional study [15] and one retrospective observational study [16]. Of the 737 patients included in the studies (average age range, 48.0-81.6 years) with advanced kidney disease, 405 received RRT including HD and PD and 332 patients received conservative management or palliative care. Patients who received conservative management were not on dialysis at the time of recruitment. In most studies, slightly more than half of the patients were male in both the RRT and conservative management groups (Table 1).

As shown in Table 2, no difference was found between the dialysis and conservative management groups with respect to psychological outcomes, but the conservative management group appeared to have more comorbidities. Three articles reported a KPS [14, 16, 21], with the median score ranging between 60 and 70 in the dialysis group and between 43 and 60 in the conservative management group. One article [14] reported HADS and SWLS scores, and scores of both survey instruments were similar for the dialysis and conservative management groups. Comorbidities appeared to be similar between conservative management and dialysis groups in the study by Seow *et al.* [21], but were higher in the conservative management group compared with the dialysis group in the other three studies [14-16].

FIGURE 1. Flow chart for study selection

TABLE 1. Characteristics of the four included studies

Reference number	1st author, year	Type of study	Stage of CKD	Intervention	No. of patients	Gender, males (%)	Age (mean $\pm$ SD)
21	Seow, 2013	Prospective observational study (a longitudinal study)	End-stage renal disease	RRT	38	20 (52.6)	71*
				Conservative	63	35 (55.6)	78*
14	Da Silva-Gane, 2012	Prospective cohort study (a longitudinal study)	Advanced CKD	Hemodialysis	80	61 (76)	60.6 $\pm$ 14.9
				Peritoneal Dialysis	44	22 (50)	48.0 $\pm$ 15.6
				Conservative Management	30	21 (70)	77.5 $\pm$ 6.5
				Not decided	16	9 (56)	68.3 $\pm$ 16.4
15	Yong, 2009	Prospective cross-sectional study	End-stage renal disease	Dialysis group	134	71 (53.0)	58.2 $\pm$ 11.4
				Palliative-care group	45	21 (46.7)	73.1 $\pm$ 7.1
16	De Biase, 2008	Retrospective observational study	End-stage renal disease	Dialysis group	5	NA	79.4
				Conservative group	11		81.5

Abbreviations: CKD, chronic kidney disease; RRT, renal replacement therapy; SD, standard deviation; NA: not available.

TABLE 2. Summary of psychological outcomes and comorbidities reported in the included studies

Reference number	1st author, year	Dialysis group	Conservative management group	Comorbidities
21	Seow, 2013	KPS: 60 (50, 80)	KPS: 60 (40, 70)	CCI: HD, 5 (5, 6); CM, 5 (3, 5)
14	Da Silva-Gane, 2012	KPS > 70: 66 (82.5%) HADS: anxiety: 5.5 $\pm$ 3.6 depression: 6.1 $\pm$ 4.0 SWLS: 21.7 $\pm$ 8.0	KPS > 70: 43 (98%) HADS: anxiety: 4.7 $\pm$ 4.0 depression: 6.4 $\pm$ 4.2 SWLS: 22.5 $\pm$ 7.3	Comorbidity: Low: HD: 65%, PD: 86%, CM: 26% High: HD: 35%, PD: 14%, CM: 74%
15	Yong, 2009	NA	NA	CCI: HD, 6.1 (2.4); CM, 8.9 (1.9)
16	De Biase, 2008	KPS: 70 (90-50)	KPS: 63.6 (50-90)	Number of comorbidities: HD: 2.6 (2-4); CM: 5.7 (3-8)

Abbreviations: CCI, Charlson comorbidity index; CM, conservative management; HADS, hospital anxiety and depression score; HD, hemodialysis; KPS, Karnofsky performance score; NA: not available; PD, peritoneal dialysis; SWLS, satisfaction with life scale.

Primary outcome measure: health-related QoL

The results of health-related QoL assessments of the four included studies are summarized in Table 3. Three studies used the SF-36 [14-16] and one study used the KD QoL-SF (version 1.2) [21]. Two studies that used the SF-36 [15, 16] did not show baseline scores and mean changes for both physical components and mental components. At the end of intervention, the dialysis group scored higher in terms of most physical components (physical function and body pain), while the conservative management group scored better than the dialysis group with regard to "role limitation due to physical health". The conservative management group scored similar to,

or better than, the dialysis group for social functioning and mental health scores, and these scores increased significantly over time. Da Silva-Gane et al. [14] did not present post-intervention data, but the mean changes in physical and mental component scores after intervention were calculated. There were no significant change in physical component scores (mean change = 0.49 $\pm$ 1.7; p = 0.53) and mental component scores (mean change = -0.69 $\pm$ 5.8; p = 0.53) in the dialysis group. There were no significant change in physical component scores (change over time = 0.04 $\pm$ 0.17), but mental component scores increased significantly over time (0.12 $\pm$ 0.32, p < 0.05) in the conservative management group. Dialysis

TABLE 3. Health-related quality of life findings of the included studies

Reference number	1st author, year	Health-related QoL tool	Scale	Subscale	Type of intervention	Before intervention*	Two years after intervention*	Descriptive findings
21	Seow, 2013	KD QoL-SF	PCS		Dialysis	33 (28, 39)	37 (30.5, 39.5)	Stabilized after dialysis started
					CM/Palliative care	34 (31, 37)	27 (24, 38)	Stable within 1.5 years, but dropped since 2 years
			MCS		Dialysis	43 (38, 49.5)	55 (48, 60.5)	
					CM/Palliative care	52 (44, 62)	58.5 (52, 60.5)	Higher scores than dialysis group in both before and after dialysis.
14	Da Silva-Gane, 2012	SF-36	PCS		Hemodialysis	25.2 ± 8.8	Mean change = 0.49 ± 1.7; p = 0.53	No change over time; no change in physical health upon dialysis initiation.
					Peritoneal dialysis	30.1 ± 6.5	NA	
					CM/Palliative care	18.0 ± 8.8	Change over time = 0.04 ± 0.17	
			MCS		Hemodialysis	47.6 ± 10.7	Mean change = -0.69 ± 5.8; p = 0.53	A significant increase over time; a decrease in mental status scores upon dialysis initiation, which was not significant.
					Peritoneal dialysis	45.9 ± 10.6	NA	
					CM/Palliative care	49.9 ± 9.9	Change over time = 0.12 ± 0.32; p < 0.05	
15	Yong, 2009	SF-36	PCS	PF	Dialysis	NA	55.9 ± 27.5	NA
					CM/Palliative care		43.8 ± 34.2	
				RP	Dialysis		42.5 ± 45.0	
					CM/Palliative care		53.3 ± 49.0	
				BP	Dialysis		75.2 ± 25.8	
					CM/Palliative care		72.8 ± 28.3	
				GH	Dialysis		38.2 ± 19.4	
					CM/Palliative care		42.4 ± 22.5	
			MCS	VT	Dialysis	NA	51.2 ± 21.4	NA
					CM/Palliative care		49 (27.08)	
				SF	Dialysis		65.80 (22.58)	
					CM/Palliative care		73.61 (24.01)	
				RE	Dialysis		50.50 (46.19)	
					CM/Palliative care		68.88 (45.72)	
				MH	Dialysis		67.10 (18.77)	
					CM/Palliative care		73.48 (19.28)	
16	De Biase, 2008	SF-36	PCS	PF	Dialysis	NA	45	NA
					CM/Palliative care		28	
				RP	Dialysis		15	
					CM/Palliative care		25	
				BP	Dialysis		62.4	
					CM/Palliative care		46.8	
				GH	Dialysis		46.2	
					CM/Palliative care		41	
			MCS	VT	Dialysis	NA	51	NA
					CM/Palliative care		47	
				SF	Dialysis		75	
					CM/Palliative care		77.4	
				RE	Dialysis		60	
					CM/Palliative care		39.8	
				MH	Dialysis		67.2	
					CM/Palliative care		67.2	

Abbreviations: BP, bodily pain; CKD, chronic kidney disease; CM, conservative management; ESRD, end-stage renal disease; GH, general health; IQR, interquartile range; MCS, mental component summary; MH, mental health; NA: not available; PCS, physical component summary; PF, physical function; RE, role limitation due to an emotional problem; RP, role limitation due to physical health; RRT, renal replacement therapy; SF, social functioning; VT, vitality.

* Data were mean +/- SD or median with IQR.

resulted in a decrease in mental status scores over time, but the results failed to reach significance.

In the study that used the KD QoL-SF (version 1.2), Seow *et al.* [21] showed that both the physical and mental component scores were unchanged by intervention in the dialysis group; however, the physical components survey score declined ($p = 0.047$), and mental components survey score increased ($p = 0.033$), in the conservative treatment group.

Quality assessment

Results of quality assessment using NOS found that all four studies scored between 6 and 9 (average score: 7.3), indicating that the studies were of good quality. All included studies earned one star for being representative of the average age in the community, and one star for being drawn from the same community as the exposed cohort. All had secure records, and did not state the outcome of interest at the start of study. For assessment of outcome, only one study had record linkage, whereas the others used self-reports for assessment of outcome.

Discussion

Our systematic review included four studies, and the major finding was that the conservative management group scored equal to or better than the dialysis group with respect to mental health-related QoL, regardless of the survey instrument used. In addition, health-related QoL significantly increased over time in patients receiving conservative management [14], suggesting that patients receiving conservative management were able to maintain their health-related QoL when compared with patients on dialysis.

Many patients with ESRD experience adjustment crises at major transition points in the course of their disease. Health-related QoL assessment is an appropriate yardstick to determine whether dialysis or conservative management can smooth this difficult transition for ESRD patients. A previous report demonstrated that health-related QoL in HD patients was lower when compared with the same CKD cohort before dialysis [19]. Another report found that SF-36 scores of CKD patients were higher in a continuous ambulatory PD group as compared with both patients receiving conservative management and those receiving HD [18]. A systematic review of 13 studies, which included three studies that reported health-related QoL data, found a similar health-related QoL between patients treated with dialysis vs. conservative care [20]. Although several studies have addressed the health-related QoL issues in patients undergoing dialysis in a CKD cohort [28-32], only a few studies have compared

health-related QoL measures between ESRD patients undergoing conservative management vs. hemodialysis. This review represents the most up-to-date information regarding this important topic.

Although comorbidities were similar between groups in one study included in our systemic review [21], they were higher in the conservative management group compared with dialysis group in the other three studies [14-16]. These findings support the notion that for some dependent patients with poor performance status and a high comorbid load, conservative management may offer an alternative to dialysis [12, 27]. Patients with worsening CKD should be evaluated by a multidisciplinary team that includes geriatric specialists to assess the medical, social and family environment prior to making any decisions regarding dialysis vs. conservative treatment [33, 34]. Non-dialysis therapy provided by a multidisciplinary nephrology team can offer comparable survival rates to dialysis, without sacrificing health-related QoL [12, 33]. In particular, several researchers have demonstrated that the emotional investment of patients and health care professionals in life-prolonging RRT in some patients may cause unnecessary (and invasive) testing, procedures and hospitalizations, with only marginal benefit [35-37].

Our study had several limitations, including the small number of studies included in the review. Of more than 300 original articles that were identified, we found only four studies that contained a health-related QoL survey. As a result, it was difficult to detect significant differences between dialysis vs. conservative management groups within these studies. Although patients who received conservative management were not on dialysis at the time of recruitment, whether the patients in the conservative/palliative management groups had received prior dialysis was not specified in the articles. In one study, all patients were initially receiving conservative therapy despite eligibility for dialysis based on standard accepted criteria [16]. Both the type of dialysis (HD and PD) and the biochemical parameters are known to affect patient health-related QoL scores, but the number of studies and the number of patients was small, which may explain why we were unable to identify significant differences based on the type of dialysis or the biochemical parameters (data not shown). Finally, two different health-related QoL scores were used in the four studies evaluated, which may have affected comparisons of the results.

In conclusion, while dialysis may appear to offer a better health-related QoL compared with conservative management, this may not always be the case. For some ESRD patients, although conservative management may be associated

with worse outcomes and a higher comorbidity load compared with dialysis, it may be superior in terms of mental health-related QoL. Thus, every patient deserves to be well-informed of all options and potential outcomes before embarking on dialysis vs. conservative management.

In addition, conservative management may not improve physical health-related QoL. This concern may be addressed by implementing a physical-related self-management or nursing care program concomitant with the conservative management. Future research involving larger cohorts of patients is required to provide a better understanding of the preferences and priorities of patients with ESRD in choosing conservative management or dialysis.

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