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NEPHROLOGY - ORIGINAL PAPER

Predicting technique and patient survival over 12 months in peritoneal dialysis: the role of anxiety and depression

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Abstract
Background Emotional distress is common in dialysis patients, but its role on clinical outcomes for patients on peritoneal dialysis (PD) is uncertain.
Purpose To evaluate the effect of depression and anxiety on 1-year prognosis in PD patients.
Methods A total of $N = 201$ PD patients (58.9 ± 12.59 years) completed the Hospital Anxiety Depression Scale and measures of social support at baseline and were followed up for CC technique and actuarial patient survival.
Results Mortality and technique failure rates were 9.9 and 5.97 %, respectively. Carer-assisted PD, anxiety, comorbid burden and albumin were significant univariate predictors. Multivariate proportional hazard model to adjust for confounders indicated that anxiety remained significant with HR of 2.145 [95 % CI 1.03, 4.49, $p = 0.043$] for death/technique failure.
Conclusion Anxiety is an important predictor of actuarial and technique survival in PD. Effective treatment for symptoms of anxiety may represent an easily achievable means of improving the clinical outcome of PD patients.

Keywords Peritoneal dialysis · Depression · Anxiety · Clinical outcomes · Technique and patient survival

Introduction

The increasing number of patients requiring treatment for end-stage renal disease (ESRD) have led to widespread efforts to promote home-based dialysis. The utilization of home-based dialysis such as peritoneal dialysis (PD), however, remains low relative to hemodialysis [1]. PD offers many potential benefits including increased autonomy and flexibility for patients, better preservation of kidney function and cost savings [2, 3], but it has also been shown to be associated with high emotional distress [4]. Distress has been shown to be associated with poor quality of life, but its role on clinical outcomes for patients on peritoneal dialysis is uncertain [5, 6].

Despite improvements in peritoneal dialysis techniques, there has been little change in patient and technique survival rates. Most studies on risk factors for poor clinical outcomes in PD patients focus on comorbidities (mainly diabetes and cardiovascular disease), residual renal function, inflammation and nutrition [7–9]. Consideration of the role of psychosocial factors such as symptoms of distress and perceived social support on PD outcomes is limited despite evidence for their prognostic value for mortality in hemodialysis [10, 11]. The purpose of this prospective single-cohort study was to evaluate the effect of depression, anxiety and social support on 1-year prognosis (patient and technique survival) in PD patients.

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Methods

Participants

Participants were consecutively recruited from 2010 to 2011 from Singapore General Hospital, Singapore, if (1) they were aged ≥21, (2) on PD for at least 3 months, (3) not hospitalized at the time of assessment or the preceding 3 weeks, (4) no dementia or psychiatric diagnosis and (5) able to communicate in English, Mandarin or Malay. Patients were free to choose their preferred language of questionnaires (English, Malay or Mandarin). The study was approved by Centralized Institutional Review Board, SingHealth Research Facilities (reference number: 2010/588/E), and informed consent was obtained.

Measures

Study participants completed the Hospital Anxiety Depression Scale [12] and measures of social support (i.e., Kidney Disease Quality Of Life Short Form; KDQOL-SF subscales [13]: social support, quality of social interaction, staff encouragement) at baseline and were followed up for 1 year for technique and actuarial patient survival.

Both the KDQOL-SF [14] and the HADS have been linguistically validated in both Mandarin and Malay [15, 16], which is a paramount consideration for use in the local context to ensure fair representation of Singaporean population. Given the linguistic diversity in our sample [$N = 104$ (51.7 %) patients completed the English HADS, $N = 29$ (14.5 %) the Malay version of HADS, and $N = 68$ (33.8 %) the Mandarin HADS], we opted for the general cutoffs for classification of anxiety and depression as these have been well validated across a range of patient populations, cultures and languages [17]. Dialysis-specific cutoff thresholds have yet to be established conclusively in other languages with recent validation studies proposing different cutoff scores ranging from 6 to 8 [18, 19].

Demographic information on age, gender, relationship status, race/ethnicity, employment status, educational level and household monthly income was captured with self-report. Laboratory parameters (e.g., albumin) and clinical data (e.g., dialysis adequacy, dialysis vintage, PD dose/regimes, comorbidities) and characteristics (e.g., PD modality; assisted PD status) were extracted from medical records at study enrollment. Comorbidities were also abstracted using the Charlson comorbidity index [20].

Clinical endpoint

The primary endpoint was the combined event of all-cause mortality and PD technique failure. Survival time was calculated as number of months from baseline assessment (time 0) until one of the following: death, switch to hemodialysis, kidney transplant, transfer out of the facility or end of the study observation period (February 2012, at a maximum of 29 months; $M = 13.58 \pm 5.27$). Status was monitored and verified through medical records and primary renal physician. For sensitivity analyses (patient and technique), survival times were also calculated based on the date of initiation onto PD (time 0) and analyses were repeated using the continuous anxiety and depression scores.

Statistical analyses

Mean ± standard deviation or percentage was determined for patient demographics, baseline clinical/laboratory results and outcomes, as appropriate. The differences between distress subgroups (as per clinical cutoffs) were analyzed by Chi-square test for categorical variables and by one-way analysis of variance test for continuous variables. Statistical procedures included Kaplan–Meier survival curves and Cox regressions. Variables associated with the combined clinical endpoint in the univariate analyses were considered for multivariate modeling. Multivariate Cox proportional-hazards model was performed to assess the relations between the combined adverse outcome and depression, anxiety controlling for significant sociodemographic, clinical covariates. Effects were considered significant when the p value was less than .05. All analyses were performed by using the SPSS version 22.

Results

Study sample

Of those eligible ($N = 241$), a total of 201 PD patients (age, 58.9 ± 12.59 years; 45 % men) were studied (response rate 83.3 %). A total 59.7 % of the participants were indicated with depression and 41.5 % with anxiety at baseline based on recommended clinical cutoff of ≥8. Patient characteristics of the total sample stratified by depression and anxiety are presented in Table 1.

Symptoms of anxiety and depression were highly interrelated ($r = .80$; $p = 0.001$). Patients with scores above the cutoffs had lower education, were more likely to be employed and with more comorbidities as per CCI relative to those with score below cutoffs. Significant difference in age was noted only between the depression subgroups with those with lower scores being significantly older than patients above depression cutoffs.

During the 12 ± 8.1 month follow-up, $N = 20$ patients died ($N = 11$ Cardiovascular deaths) and $N = 12$ switched to hemodialysis due to technique failure. The most frequent causes of death were cardiovascular events and/or sepsis, whereas most frequent causes of transfer to HD were peritonitis and/or sepsis. Mean survival time was 13.6 ± 5.27 months.

Table 1 Demographics and clinical characteristics of total sample stratified based on symptoms of depression and anxiety

	Total sample	Depression (HADS)		Anxiety (HADS)	
	($N = 201$)	Above cutoff	Below cutoff	Above cutoff	Below cutoff
	M ± SD/*N* (%)	M ± SD/*N* (%)	M ± SD/*N* (%)	M ± SD/*N* (%)	M ± SD/*N* (%)
Age (years)	58.92 ± 12.59	56.11 ± 8.21**	59.18 ± 7.47**	58.21 ± 3.22	57.13 ± 7.36
Gender (male)	90 (45)	51 (54)	60 (46)	54 (48)	57 (52)
Ethnicity (Chinese)	151 (75)	80 (53)	71 (47)	82 (54)	69 (46)
Education level					
Primary	78 (38)	45 (57)*	33 (43)*	47 (60)*	32 (40)*
Secondary	81 (40)	40 (49)	41 (51)	41 (51)	40 (49)
Tertiary	42 (22)	18 (43)	24 (57)	16 (38)	26 (62)
Marital status (married)	146 (72)	70 (48)	76 (52)	72 (49)	74 (51)
Employed	46 (23)	30 (65)*	16 (35)*	33 (71)**	13 (29)**
Income[a] (<S$2000)	86 (56)	40 (46)	46 (54)	42 (48)	44 (52)
PD modality					
APD	86 (42)	42 (49)	44 (51)	44 (51)	42 (49)
CAPD	115 (48)	54 (47)	61 (53)	51 (44)	64 (56)
Carer-assisted PD					
Assisted	62 (30)	30 (49)	32 (51)	38 (61)	24 (39)
Self-care	139 (70)	68 (48)	71 (52)	72 (52)	67 (48)
Medication (total count per day)	8.20 ± .8	8.73 ± .7**	7.80 ± .9**	8.53 ± 1.5**	7.91 ± 1.1**
PD vintage (months)	41.85 ± 31.85	40.11 ± 30.02	42.01 ± 32.02	41.44 ± 31.02	41.92 ± 32.21
CCI	5.60 ± 1.92	5.80 ± 1.92*	5.42 ± 1.83*	5.92 ± 1.78**	5.33 ± 2.04**
Self-report comorbidities	4.10 ± .32	3.99 ± .22**	4.32 ± .43**	3.82 ± .58**	4.36 ± 1.02**
Hypertension	192 (95)	118 (57)	84 (43)	111 (57)	81 (43)
Cardiac disease	6 (2)	4 (66)	2 (34)	3 (50)	3 (50)
Cerebrovascular	19 (9)	11 (58)	8 (42)	10 (52)	9 (48)
Diabetes (preexisting)	84 (42)	39 (46)	45 (54)	40 (48)	44 (52)
Potassium (mmol/I)	4.74 ± .79	4.59 ± .91	4.81 ± .72	4.65 ± .84	4.74 ± .77
Phosphate (mmol/I)	1.88 ± .51	1.83 ± .44	1.91 ± .50	1.87 ± .53	1.88 ± .52
Albumin (g/dl)	2.93 ± .51	2.91 ± .55	2.94 ± .49	2.92 ± .52	2.93 ± .50
Hemoglobin (g/dl)	10.83 ± 1.62	11.10 ± 1.83**	10.33 ± 1.44**	10.98 ± 1.66	11.13 ± 1.59
Kt/V	2.40 ± .32	2.38 ± .28	2.42 ± .36	2.45 ± .42	2.50 ± .28

Data expressed as M ± SD or *N* (%),* $p \leq 0.05$, ** $p \leq 0.01$

CCI Charlson comorbidity index, *ESRD* end-stage renal disease

[a] $N = 154$ as $N = 16$ participants ticked option 'do not wish to answer' for income and $N = 35$ indicated 'do not know'

Factors associated with clinical outcomes

Univariate analyses indicated that assisted PD, anxiety, Charlson comorbidity index, primary diagnosis of diabetic nephropathy, and albumin were associated with actuarial/technique survival (Table 2). Survival rates were 90 % for non-anxious patients and 76.5 % for those with anxiety (log-rank $\chi^2 = 7.12$; $p = 0.003$). The effect of depression approached, but did not reach significance ($p = 0.06$). None of the remaining demographic, laboratory/clinical parameters or social support indicators were significant.

Multivariate proportional hazard model to adjust for sociodemographic and clinical characteristics indicated that anxiety remained independently associated with all-cause mortality/technique (HR 2.25 [95 % CI 1.09, 4.63, $p = 0.02$]). Albumin and CCI were also associated with increased risk for all-cause mortality/technique failure in the multivariate model (Table 2). Sensitivity analysis using survival times calculated based on PD initiation rather than study entry/baseline yielded similar results (HR for anxiety = 2.54 [95 % CI 1.19, 5.42, $p = 0.02$]). Effects also remained significant in analysis using the continuous

Table 2 Unadjusted and adjusted multivariate Cox regression analyses

Variables	Unadjusted		Adjusted multivariate model[c]	
	Combined endpoint (mortality; technique failure)		Combined endpoint (mortality; technique failure)	
	HR (95 % CI)	*p* value	HR (95 % CI)	*p* value
Age (years)	1.023 (.993–1.053)	.130		
Gender (male)	.720 (.350–1.474)	.369		
Ethnicity (non-Chinese)	.753 (.350–1.591)	.457		
Education (primary or lower)	1.568 (.559–4.399)	.393		
Marital status (married)	.710 (.342–1.473)	.358		
Employed (yes)	.463 (.178–1.203)	.114		
Income (< S$ 2,000)[a]	.989 (.439–2.228)	.979		
PD modality (APD)	1.098 (.546–2.208)	.793		
Carer-assisted PD (yes)	2.362 (1.176–4.744)	.016	1.181 (.530–2.631)	.684
PD vintage (months)	1.001(.991–1.009)	.995		
Medication (total count per day)	1.104 (.965–1.264)	.149		
CCI[b]	1.323 (1.113–1.578)	.002	1.261 (1.052–1.512)	.012
Number of comorbidities[b] (self-report)	1.126 (.924–1.627)	.157		
Hypertension (yes)	1.271 (.303–5.327)	.743		
Cardiac disease (yes)	1.694 (.231–12.413)	.604		
Cerebrovascular disease (yes)	3.967 (1.778–8.853)	.001		
Diabetes preexisting (yes)	2.428 (1.887–4.968)	.015	1.367 (.611–3.056)	.447
Albumin (g/L)	.895 (.843–.950)	.0001	.900 (.845–.958)	.001
Hemoglobin (g/dL)	1.033 (.829–1.289)	.771		
Potassium (mmol/I)	.607 (.354–1.039)	.068		
Phosphate (mmol/I)	.764 (.387–1.509)	.439		
Kt/V	1.198 (.793–1.809)	.397		
Quality of social interaction	.987 (.983–1.025)	.690		
Staff encouragement	1.004 (.996–1.017)	.500		
Social support	.996 (.980–1.021)	.630		
Anxiety (yes)	2.560 (1.251–5.237)	.01	2.252 (1.094–4.634)	.028
Depression (yes)	2.071 (.930–4.611)	.065		

HR > 1 indicates increasing risk of death/technique failure with increasing predictor values (continuous predictor) or with the presence of a condition (binary predictor) and vice versa

HR hazard ratio, *CI* confidence interval, *PD* peritoneal dialysis, *CCI* Charlson comorbidity index

[a] $N = 154$ as $N = 16$ participants ticked option 'not wish to answer' for income and $N = 35$ indicated 'do not know'

[b] Natural logarithmic transformation of the variable

[c] Multivariate model backward conditional entry including only variables with significant univariate associations with death/technique failure combined endpoint

anxiety scores rather than clinical cutoffs (HR = 1.09, [95 % CI 1.02, 1.12, $p = 0.01$]).

Discussion

This is the first prospective study to explore the role of psychological parameters as risk factors for death and technique failure in patients on peritoneal dialysis.

Several important findings are evident from this study. Firstly, anxiety and depressive symptoms are common in PD patients and require attention. The majority of our patients experienced symptoms of depression or anxiety or both that have been shown in previous work to be related to treatment disruptiveness [21].

Although anxiety and depression are highly comorbid, only anxiety emerged as a (stronger) independent predictor of actuarial and technique survival in PD patients. The

effect remained significant even after adjustment for other risk factors, in line with some of the evidence on myocardial infarction patients [22].

Notably, the risk conferred was higher than those of traditional clinical risk factors. Anxiety may exert an effect on prognosis through compromised health behaviors or physiological pathways such as reduced heart rate variability [23] and/or stress-induced increases in sympathetic nervous system activities and catecholamine release, which are linked to cardiovascular strain. Furthermore, PD patients have significantly increased norepinephrine plasma levels [24], which ex vivo work has shown to reduce ionic permeability of the peritoneal membrane pertinent to deterioration of PD technique efficacy [25] and thereby technique failure.

More work is needed to elucidate mechanisms and replicate findings with larger samples. This preliminary work, however, supports the call for screening and interventions integrated in routine renal care to improve emotional outcomes in end-stage renal disease and in PD in particular. Symptoms of anxiety have received less attention in both research and clinical practice. Regular assessment of distress symptoms (not confined to depression) may help to identify at risk patients who will benefit from treatment and/or referral to psychological services. Effective treatment for symptoms of distress may represent an easily achievable means of improving both quality of life and the clinical outcome of PD patients. Several limitations need to be recognized including the observational design that precludes causal inferences, the small sample size and number of death/events that made the derivation of combined events endpoint necessary, the lack of serial assessments of emotional distress over study window and the use of self-reported measurement of symptoms of anxiety and depression rather than diagnostic interviews.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Jiwakanon S, Chiu YW, Kalantar-Zadeh K, Mehrotra R (2010) Peritoneal dialysis: an underutilized modality. Curr Opin Nephrol Hypertens 19(6):573–577
2. Tam P (2009) Peritoneal dialysis and preservation of residual renal function. Perit Dial Int 2(2):S108–S110
3. Klarenbach S, Manns B (2009) Economic evaluation of dialysis therapies. Semin Nephrol 29(5):524–532
4. Griva K, Kang AWC, Yu ZL et al (2014) Quality of life and emotional distress between patients on peritoneal dialysis versus community-based hemodialysis. Qual Life Res 23(1):57–66
5. Chilcot J, Wellsted D, Farrington K (2009) Depression in end-stage renal disease: current advances and research. Semin Dial 23:74–82
6. Cukor D, Ver Halen N, Fruchter Y (2013) Anxiety and quality of life in ESRD. Semin Dial 26(3):265–268
7. Davies SJ, Russell L, Bryan J, Phillips L, Russell GI (1995) Comorbidity, urea kinetics, and appetite in continuous ambulatory peritoneal dialysis patients: their interrelationship and prediction of survival. Am J Kidney Dis 26:353–361
8. Jager KJ, Merkus MP, Dekker FW et al (1999) Mortality and technique failure in patients starting chronic peritoneal dialysis: results of the Netherlands Cooperative Study on the Adequacy of Dialysis. NECOSAD Study Group. Kidney Int 55:1476–1485
9. Stenvinkel P, Chung SH, Heimburger O, Lindholm B (2001) Malnutrition, inflammation, and atherosclerosis in peritoneal dialysis patients. Perit Dial Int 21(3):S157–S162
10. Fan L, Sarnak MJ, Tighiouart H et al (2014) Depression and all-cause mortality in hemodialysis patients. Am J Nephrol 40(1):12–18
11. Thong MS, Kaptein AA, Krediet RT, Boeschoten EW, Dekker FW (2007) Social support predicts survival in dialysis patients. Nephrol Dial Transplant 22(3):845–850
12. Zigmond AS, Snaith RP (1983) The hospital anxiety and depression scale. Acta Psychiatr Scand 67(6):361–370
13. Hays RD, Kallich JD, Mapes DL et al (1997) Kidney disease quality of life short form (KDQOL-SF ™). Version 1.3: a manual for use and scoring. Rand, Santa Monica
14. RAND Health. Kidney disease quality of life instrument (KDQOL). http://www.rand.org/health/surveys_tools/kdqol.html. Accessed 22nd November 2015
15. Leung CM, Ho S, Kan CS, Hung CH, Chen CN (1993) Evaluation of the Chinese version of the hospital anxiety and depression scale: a cross-cultural perspective. Int J Psychosom 40(1–4):29–34
16. Yusoff N, Low WY, Yip CH (2011) Psychometric properties of the Malay version of the hospital anxiety and depression scale: a study of husbands of breast cancer patients in Kuala Lumpur, Malaysia. Asian Pac J Cancer Prev 12(4):915–917
17. Bjelland I, Dahl AA, Haug TT, Neckelmann D (2002) The validity of the hospital anxiety and depression scale: an updated literature review. J Psychosom Res 52(2):69–77
18. Loosman WL, Siegert CEH, Korzec A, Honig A (2010) Validity of the hospital anxiety and depression scale and the beck depression inventory for use in end-stage renal disease patients. Br J Clin Psychol 49(4):507–516
19. Preljevic VT, Østhus TBH, Sandvik L, Opjordsmoen S, Nordhus IH, Os I, Dammen T (2012) Screening for anxiety and depression in dialysis patients: comparison of the hospital anxiety and depression scale and the beck depression inventory. J Psychosom Res 73(2):139–144
20. Charlson ME, Pompei P, Ales KL, MacKenzie CR (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 40(5):373–383
21. Griva K, Davenport A, Harrison M, Newman S (2010) An evaluation of illness, treatment perceptions, and depression in hospital vs. home-based dialysis modalities. J Psychosom Res 69(4):363–370

22. Frasure-Smith N, Lesperance F, Talajic M (1995) The impact of negative emotions on prognosis following myocardial infarction: is it more than depression? Health Psychol 14:388–398
23. Thayer JF, Friedman BH, Borkovec TD (1996) Autonomic characteristics of generalized anxiety disorder and worry. Biol Psychiatry 39:255–266
24. Vlachojannis JG, Tsakas S, Alexandri S, Petropoulou C, Goumenos DS (2000) Continuous ambulatory peritoneal dialysis is responsible for an increase in plasma norepinephrine. Perit Dial Int 20:322–327
25. Stefanidis I, Zarogiannis S, Hatzoglou C et al (2005) Enhancement of the transmesothelial resistance of the parietal sheep peritoneum by epinephrine in vitro: Ussing-type chamber experiments. Artif Organs 29(11):919–922