Systematic Review and Meta-Analysis

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Do psychological interventions reduce depression in hemodialysis patients?

A meta-analysis of randomized controlled trials following PRISMA

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Abstract

Background: Depression is highly prevalent in hemodialysis patients and results in poor patient outcomes. Although psychological interventions are being developed and used for these patients, there is uncertainty regarding the effectiveness of these interventions. The purpose of this meta-analysis is to evaluate the effects of psychological interventions on depression treatment in hemodialysis patients.

Methods: All randomized controlled trials (RCTs) relevant to the depression treatment of hemodialysis patients through psychological interventions were retrieved from the following databases: Embase, Pubmed, PsycINFO, the Cochrane Database of Systematic Reviews, and the Cochrane Central Register of Controlled Trials. The reference lists of identified RCTs were also screened. The Cochrane risk of bias tool was used to evaluate the quality of the studies, RevMan (5.3) was used to analyze the data, and the evidence quality of the combined results was evaluated using GRADE (3.6.1).

Results: Eight RCTs were included. The combined results showed that psychological interventions significantly reduced the scores of the Beck Depression Inventory ($P<0.001$) and interdialysis weight gain ($P<0.001$). However, due to the high heterogeneity, effect size combinations of sleep quality and quality of life were not performed.

Conclusion: Psychological interventions may reduce the degree of depression and improve fluid intake restriction adherence. More rigorously designed research is needed.

Abbreviations: ATP = adaptation training program, BAI = Beck Anxiety Inventory, BDI = Beck Depression Inventory, CBT = cognitive behavioral therapy, CDSR = the Cochrane Database of Systematic Reviews, CENTRAL = the Cochrane Central Register of Controlled Trials, CI = confidence interval, DSM IV = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, ESRD = end-stage renal disease, HADS = Hospital Anxiety and Depression Scale, IDWG = interdialysis weight gain, MBCT = music therapy and mindfulness-based cognitive therapy, MCS = Mental Component Summary, MeSH = medical subject headings, MINI = Mini-International Neuropsychiatric Interview, NICE = the National Institute for Health and Clinical Excellence, PCS = Physical Component Summary, PRISMA = the preferred reporting items for systematic reviews and meta-analysis, PSQI = Pittsburgh Sleep Quality Index, RCT(s) = randomized controlled trial(s), SCL90 = Symptom Checklist 90, SD = standard deviation, SE = standard error, SF-36 = the MOS 36-Item Short Form Health Survey, SMD = standardized mean difference, SUPPH = Strategies Used by People to Promote Health.

Keywords: depression, hemodialysis, meta-analysis, psychological intervention

1. Introduction

By 2020, the number of ESRD (end-stage renal disease) patients in the world will have increased nearly 60% compared to 2005,[1] and most of them will receive dialysis. According to statistical data from the United States, more than 400,000 ESRD patients in the United States in 2011 were receiving hemodialysis,[2] and in Saudi Arabia, the proportion of ESRD patients receiving hemodialysis was as high as 92.8%.[1]

Editor: Pavlos Malindretos.

Funding: This work was funded by the science and technology plan projects in Sichuan province (2014SZ0095), which provided financial support and supervised our job schedule.

LX and RC contributed equally to this work.

The authors have no conflicts of interest to disclose.

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Medicine (2016) 95:34(e4675)

Received: 18 April 2016 / Received in final form: 20 July 2016 / Accepted: 22 July 2016

http://dx.doi.org/10.1097/MD.0000000000004675

Hemodialysis patients are prone to a variety of psychological problems. Depression is the most common of these psychological problems, with a morbidity rate that can reach 25%, 4 times the rate among normal populations.[3] Depression in hemodialysis patients may cause many problems, including the following: treatment adherence reduction,[4] especially dietary and fluid intake restriction adherence,[5] with a 14.4% to 67% rate of nonadherence[6]; sleep disturbance,[7] the incidence of which is 40% to 85% among hemodialysis patients,[8,9] higher than in normal populations; and depression in hemodialysis patients can increase the hospitalization rate, increase the incidence of heart diseases, exacerbate sexual dysfunction, reduce quality of life, and increase mortality.[10–12] Therefore, it is essential to take effective and timely measures to reduce depression in hemodialysis patients.

As a complementary therapy, psychological intervention can prevent the problems of side effects and low adherence in comparison to drug therapy[13,14] and is easier for patients to accept. In addition, some studies have confirmed the effectiveness of psychological intervention in reducing the risk of depression relapse.[15,16] Thus, NICE (the National Institute for Health and Clinical Excellence) recommends psychological intervention, and increasing numbers of hemodialysis patients with depression are treated with psychological interventions.[17] However, the efficacy of psychological intervention is still debated by some scholars. Krespi et al[18] reported that specific imagery intervention could not effectively improve quality of life and adjust emotion during posttreatment or at follow-up. Matthews et al[19] showed that neither intercessory prayer nor transpersonal positive visualization affected dialysis patients' well-being. Therefore, whether psychological interventions are effective to treat depression in hemodialysis patients remains to be confirmed. This issue has not been summarized in any previous systematic review or meta-analysis.

The present systematic review and meta-analysis aims to summarize and evaluate the effects of psychological interventions on the reduction of hemodialysis patients' degree of depression and on improvements to sleep quality, fluid intake restriction adherence, and quality of life. The results can provide medical facilities and dialysis centers with an evidence-based basis for establishing new systems and practices in clinics.

2. Methods

The protocol of this meta-analysis was registered in PROSPERO (CRD42016037063) (www.crd.york.ac.uk/prospero). All analyses were based on previously published studies; thus, ethical approval and patient consent were not necessary.

2.1. Study selection

All the studies were screened and selected by 2 independent review authors (RC and YD). The prespecified eligibility criteria were as follows: types of studies: RCTs (randomized controlled trials) that compared psychological interventions with a control group in the treatment of depression in hemodialysis patients; types of participants: hemodialysis-dependent patients aged above 18 and diagnosed with depression. We accepted each individual trial's criteria for depression diagnosis and the exclusion criteria of participants; types of psychological interventions: treatment of depression without pharmacological interventions and with any psychological interventions were included, such as CBT (cognitive behavioral therapy), rational-emotive therapy, and ATP (adaptation training program); types of control groups: a control psychological intervention, supportive treatment, usual care or no treatment were included; types of outcome measures: degree of depression of interventional and control groups must be evaluated at posttreatment (for any measure used); sleep quality, fluid intake restriction adherence, and quality of life could also be included (for any measure used); sample size: sample sizes of 10 or more; type of journal: published in peer-reviewed journals; publication language: English only. If a duplicate publication was identified, we used the most relevant publication. We excluded retracted studies. After assessment, we resolved disagreements between the 2 authors through discussion with a third reviewer (XJ).

2.2. Search method

We developed and conducted a comprehensive search of published and unpublished RCTs using EMBASE (1980–March 2016), PubMed (1966–March 2016), PsycINFO (1806–March 2016), CDSR (the Cochrane Database of Systematic Reviews, 2016), and CENTRAL (the Cochrane Central Register of Controlled Trials, 2016). The search terms consisted of medical subject headings (MeSH) and keywords: (hemodialysis OR hemodialysis) AND (psychological intervention OR psychotherapy OR crisis intervention) AND depression AND (randomized controlled trial OR randomized). The PubMed search terms were: (randomized controlled trial[Publication Type] OR randomized[Title/Abstract] OR placebo[Title/Abstract]) AND ("Crisis Interventions"[Title/Abstract] OR Intervention, Crisis [Title/Abstract] OR Interventions, Crisis[Title/Abstract] OR "Critical Incident Stress Debriefing"[Title/Abstract] OR "Crisis Intervention"[Mesh]) OR (Psychotherapies[Title/Abstract] OR Psychotherapists[Title/Abstract] OR Psychotherapist[Title/Abstract]) OR "Clinical Psychotherapists"[Title/Abstract] OR "Clinical Psychotherapist"[Title/Abstract] OR Psychotherapist, Clinical[Title/Abstract] OR Psychotherapists, Clinical[Title/Abstract] OR Logotherapy[Title/Abstract] OR Logotherapies [Title/Abstract] OR "Psychotherapy"[Mesh]) OR ("mental intervention"[Title/Abstract] OR "psychological intervention"[-Title/Abstract] OR psychointervention[Title/Abstract]) OR ("Cognitive Therapies"[Title/Abstract] OR Therapies, Cognitive[Title/Abstract] OR "Cognition Therapy"[Title/Abstract] OR "Cognition Therapies"[Title/Abstract] OR Therapies, Cognition [Title/Abstract] OR "Cognitive Behavior Therapy"[Title/Abstract] OR Therapy, Cognitive Behavior[Title/Abstract] OR "Cognitive Psychotherapy"[Title/Abstract] OR "Cognitive Psychotherapies"[Title/Abstract] OR Psychotherapies, Cognitive[Title/Abstract] OR Psychotherapy, Cognitive[Title/Abstract] OR Therapy, Cognition[Title/Abstract] OR Therapy, Cognitive [Title/Abstract] OR Behavior Therapy, Cognitive[Title/Abstract] OR Behavior Therapies, Cognitive[Title/Abstract] OR "Cognitive Behavior Therapies"[Title/Abstract] OR Therapies, Cognitive Behavior[Title/Abstract] OR "Cognitive Behavioral Therapy"[Title/Abstract] OR Behavioral Therapies, Cognitive [Title/Abstract] OR Behavioral Therapy, Cognitive[Title/Abstract] OR "Cognitive Behavioral Therapies"[Title/Abstract] OR Therapies, Cognitive Behavioral[Title/Abstract] OR Therapy, Cognitive Behavioral[Title/Abstract] OR "CBT"[Title/Abstract] OR "cognitive behavior therapy"[Title/Abstract] OR "cognitive behaviour therapy"[Title/Abstract] OR "cognitive behavioral therapy"[Title/Abstract] OR "cognitive behavioural therapy" [Title/Abstract] OR "cognitive behavior therapies"[Title/Abstract] OR "cognitive behaviour therapies"[Title/Abstract]

OR "cognitive behavioral therapies"[Title/Abstract] OR "cognitive behavioural therapies"[Title/Abstract] OR "Cognitive Therapy"[Mesh]) AND (hemodialysis[Title/Abstract] OR hemodialyses[Title/Abstract] OR hemotodialysis[Title/Abstract] OR "HD"[Title/Abstract] OR "MHD"[Title/Abstract] OR "maintained hemodialysis"[Title/Abstract] OR "maintained hemodialyses"[Title/Abstract]). We also searched the reference lists of original reports, case reports, guidelines, letters to the editor, reviews, and meta-analysis retrieved through electronic searches for additional articles.

2.3. Data extraction and quality assessment

Titles and/or abstracts of studies retrieved using the search strategy and those from additional sources were screened independently by 2 review authors (RC and YD) to identify studies that potentially met the inclusion criteria outlined above. For studies that potentially fulfilled the inclusion criteria, we searched the full papers, which were assessed independently by the same 2 authors. The same 2 authors also used a predesigned data collection form (Microsoft Office Excel 2013) to extract all the data independently. The following information was collected: study design, study site, participant inclusion and exclusion criteria, criteria used to diagnose depression, sample size (2 groups and the total size), mean and standard deviation of the 2 groups, psychological interventions (method, frequency, durations of once and total intervention), control interventions, outcomes, and measures. Information used to evaluate the risk of bias for each study was also collected, including methods used to generate the randomization, allocation concealment, and blinding. The data were entered twice into RevMan. We defined the degree of depression[20–24] as our primary outcome (for any measure used). As associated symptoms of depression in hemodialysis patients, sleep quality,[21,25] IDWR (interdialysis weight gain),[20,26] and quality of life[18,23,24] were combined as secondary outcomes. IDWG was used to represent fluid intake restriction adherence in hemodialysis patients. After extraction, all data were checked by another author (XJ), and discrepancies were resolved by discussion with her. We sent letters to the authors to clarify missing or unclear data.

The risk of bias assessment was conducted independently by 2 authors (LX and JQ), and disagreements were discussed with a third author (CY). The Cochrane risk of bias tool was used for the assessment of random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. Each domain was rated as low (unlikely to seriously alter the results), unclear, or high (seriously weakens confidence in the results). The possibility of bias is minimal when all the criteria are met (grade A); grade B has a medium possibility of bias occurring; and if the criteria are not met at all, the possibility of bias is high, and the grade is C. We acknowledge that it may be impossible to achieve blinding of participants and therapists/investigators in trials using psychological interventions, only the outcome evaluator may be blinded.

2.4. Data synthesis and statistical analysis

Two review authors entered data separately (YD and JQ), and we conducted the meta-analysis using Review Manager (RevMan, Version 5.3, The Cochrane Collaboration, Copenhagen: The Nordic Cochrane Centre).

For RCTs, heterogeneity was analyzed by calculating the Chi-squared test (P of 0.05 was used for statistical significance) and the I^2 test. The higher the percentage was, the higher the level of heterogeneity.[27] If $P > 0.10$ and $I^2 < 50\%$, we considered the heterogeneity to be insufficient, and a fixed effects model was used to pool data; if $P < 0.10$ and $I^2 > 50\%$, we considered the heterogeneity to be substantial, so we used a random effects model to summarize the results. If heterogeneity was still high after adopting the random effects model, the data were not combined and were described separately, and the reasons for the heterogeneity were investigated.

Continuous data were pooled as SMD (standardized mean difference) with a 95% CI (confidence interval). We used forest plots and funnel plots. The funnel plots can indicate possible publication bias, evidence of asymmetry, and other small study effects.[28] In addition, GRADE (3.6.1, The GRADE Working Group) was used to rank the evidence quality. Because SF-36 (the MOS 36-Item Short Form Health Survey) can be divided into a PCS (Physical Component Summary) and an MCS (Mental Component Summary), we used subgroup analysis to check whether psychological interventions can separately improve physical or mental quality of life. Finally, we followed PRISMA (the preferred reporting items for systematic reviews and meta-analysis) guidelines to report our findings.[29]

3. Results

3.1. Results of the search

We identified 614 records and finally recruited 8 studies (Fig. 1). The 8 studies were RCTs involving a total of 612 hemodialysis patients for quantitative synthesis, and all were reviewed by an institutional ethics committee before implementation. Among the 612 patients, 311 and 301 patients were allocated into the intervention and control groups after randomization, respectively.

3.2. Study characteristics

The participants in the 8 RCTs were all hemodialysis patients. Of these, 5 studies[20–24] defined the degree of depression as the main outcome, but only 2 of the studies[20,22] defined depression clearly. In the other 3 studies,[21,23,24] the definition was ambiguous. Eight trials studied 4 types of psychological interventions. The most widely used psychological intervention was CBT,[20–23,25] followed by rational-emotive therapy,[26] ATP,[24] and specific visual imagery.[18] Although many psychological interventions were used, these methods had a large degree of overlap; some of these trials used a multidimensional approach to treat patients. One trial[21] used sleep hygiene education, 1 trial[22] used brief individualized psychological consultation, and another trial[18] used no treatment as a control. Standard care was performed in the other trials, which was described as routine hemodialysis, usual care, or routine nursing care in the original studies. Five trials used BDI (Beck Depression inventory) scale to assess the degree of depression, whereas Krespi[18] used HADS (Hospital Anxiety and Depression Scale). The self-report symptom inventory, SCL90 (Symptom Checklist 90), was applied in Hou's 2 trials.[25,26] In addition, 2 trials[21,25] used PSQI (Pittsburgh Sleep Quality Index) to assess sleep quality, 2 trials[20,26] used IDWG to evaluate fluid intake restriction adherence, and 3 trials[18,23,24] used SF-36 to assess quality of life and all divided the SF-36 into PCS and MCS.

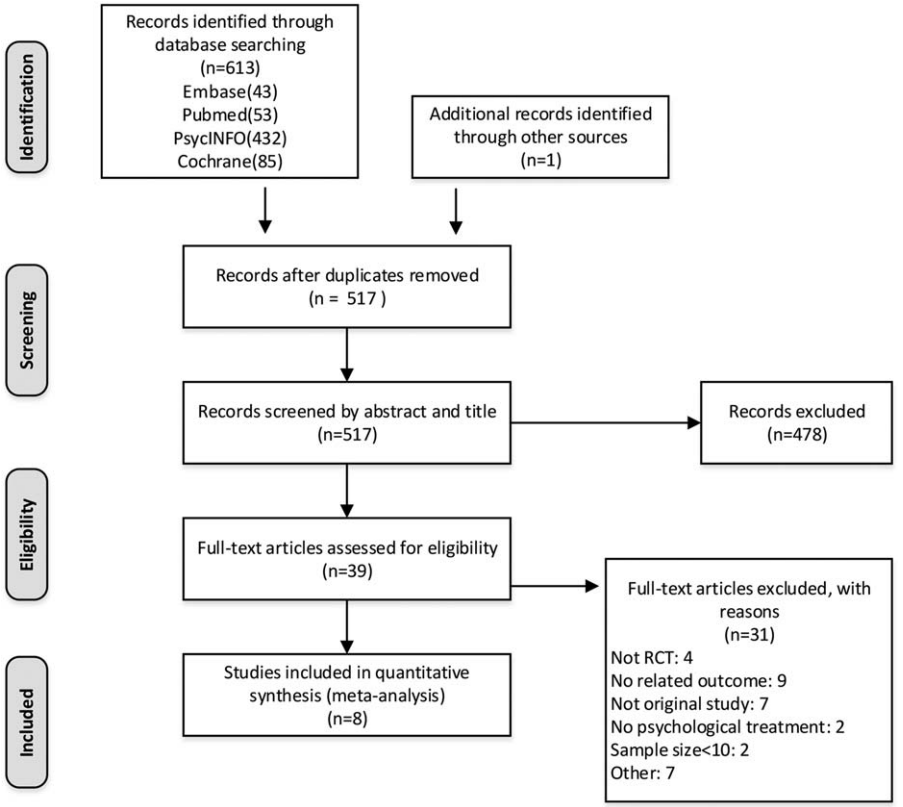

Figure 1. Study flow diagram. RCT = randomized controlled trial.

Regarding the types of psychological interventions, there were various frequencies and durations of interventions. The characteristics of the included studies are presented in Table 1.

3.3. Risk of bias in the included studies

We used the Cochrane risk of bias tool to assess the risk of bias of each study. We present them using a "Risk of bias graph" (Fig. 2) and a "Risk of bias summary" (Fig. 3). For the 8 RCTs that we included, only 1[22] was grade A, and the other studies were all grade B. All studies were described as "randomized," but only 3 of the studies reported the randomization methods and procedures in detail (37.5%). In addition, only 3 of the studies described allocation concealment in detail (37.5%), which may have produced selection bias and prevented us from assessing the influence of allocation concealment in the remaining studies. Thus, the generalization of results may have been influenced. Furthermore, because of the nature and method of implementation of psychological interventions, it was impossible to perform blinding, especially blinding of the participants and personnel. Blinding of the participants and therapists/investigators occurred in only 2 studies (25.0%), and 3 studies conducted blinding of outcome assessment (37.5%). This lack of blinding may have induced performance bias in the original articles. All studies described the drop outs and reasons, which could help to prevent attrition bias to some extent, but only 1 study[18] used intent-to-treat analysis to analyze the data (12.5%). All studies clearly reported all expected results to avoid reporting bias. Moreover, all studies reported that there were no statistically significant differences in age or sex between the intervention and control groups at baseline ($P > 0.05$). Finally, the funnel plot for the primary outcome "degree of depression" (Fig. 4) appeared to be not totally asymmetrical. However, because the number of trials included was insufficient, the assessment of publication bias may be inaccurate.

3.4. Efficacy of psychological interventions

3.4.1. Degree of depression. Five studies[20–24] involving 321 patients (161 in the intervention group and 160 in the control group) reported the effect of psychological interventions on hemodialysis patients' degree of depression, indicating a statistically significant difference between the psychological intervention and the control (SMD −0.52, 95% CI: −0.75 to −0.30; $I^2 = 20\%$, $P = 0.29$). Psychological interventions were able to effectively reduce the hemodialysis patients' degree of depression ($P < 0.001$) (Fig. 5).

3.4.2. Sleep quality. Two studies[21,25] involving 170 patients (88 in the intervention group and 82 in the control group) reported the effect of psychological interventions on hemodialysis patients' sleep quality, indicating no statistically significant difference between the psychological intervention and the control (SMD −1.07, 95% CI: −2.26 to 0.12; $I^2 = 92\%$, $P < 0.001$) (Fig. 6). Thus, psychological interventions were unable to demonstrate improvement in hemodialysis patients' sleep quality ($P = 0.08$). However, the estimate was associated with a high level of uncertainty due to severe heterogeneity after adopting a

Table 1

Characteristics of the included studies.

Study	Sample					Study design	Study site	Intervention				Control group	Outcomes	Measures
	Inclusion criteria	Exclusion criteria	Diagnosis criteria for depression	Intervention group (n)	Control group (n)			Intervention group	Frequency	Duration of once (min)	Duration of total (wk)			
Chen et al[21]	Maintenance HD: >6 mo; PSQI score of >5; aged ≥18 y old; a history of sleep disturbance for >6 mo	With active medical and psychiatric conditions	—	37	35	RCT	The Far Eastern Memorial Hospital	CBT: sleep restriction, stimulus control, relaxation training	3/wk	—	6	Sleep hygiene education	Degree of depression, anxiety, sleep quality	BDI, PSQI, BAI
Cukor et al[20]	Aged >18 y, ESRD treatment with hemodialysis for at least 6 mo and elevated depressive affect, without psychosis, current substance abuse, current ongoing psychotherapy	Current hospitalization, altered mental status (Mini score <23), a change in psychotropic medication in the past 6 mo	BDI-II score >10	33	26	RCT	Two dialysis units in Brooklyn, NY	CBT: assessment, psychoeducation, behavioral intervention, and behavioral intervention	Every time of hemodialysis	—	12	Usual standard of care	Degree of depression, IDWG	BDI, IDWG
Duarte et al[22]	Patients with ESRD receiving outpatient hemodialysis >3 mo, 18–80 y old and diagnosis of a major depressive disorder according to the MINI criteria, without cognitive impairment or mental retardation, current substance abuse	Having a living-donor renal transplant scheduled within the next several months, current hospitalization, psychiatric comorbidity diagnosed by the MINI	Major depression defined by >5 clinical criteria in the MINI	41	44	RCT	Two dialysis units in the state of São Paulo, Brazil	CBT: the self-monitoring of mood status; cognitive restructuring; programming pleasant activities; training on social abilities and assertiveness; relaxation exercises with positive imagination	1/wk	90	12	Brief individualized psychological consultation	Degree of depression	BDI
Hou et al[25]	Patients with ESRD, underwent hemodialysis >3 mo; PSQI >7; with clear consciousness; with normal intelligence (0–2 scores for the adult intelligence disability scale)	With infection or hemorrhage; psychiatric history or personality disorder	—	51	47	RCT	Hemodialysis Center of Affiliated Hospital of Guangdong Medical College	CBT: progressive muscle relaxation and sleep-related behavior modification	3 times every 2 d	20–30	12	Conventional hemodialysis	Degree of depression, anxiety, sleep quality	PSQI, SCL90
Hou et al[26]	ESRD patients who received over 3 mo of hemodialysis. With clear consciousness, with normal intelligence	With infection or hemorrhage; psychiatric history or personality disorder	—	48	44	RCT	The Affiliated Hospital of Guangdong Medical College	Rational-emotive therapy: Psychodiagnosis, Comprehension and Application	—	—	12	Routine hemodialysis	Degree of depression, anxiety, IDWG	IDWG, SCL90
Lii et al[23]	>18 y and literate in Mandarin or Taiwanese languages; diagnosed with ESRD and receiving routine hemodialysis treatment and consented to participate	Patients with history of psychiatric disorders or severe systemic diseases	—	20	28	RCT	Three hemodialysis units of 2 hospitals in northern Taiwan	Cognitive behavioral therapy and self-efficacy theory: performance accomplishment, modeling, verbal persuasion, and interpretation of physiological symptoms	1/wk	120	8	Routine nursing care	Degree of depression, quality of life, self-efficacy	BDI, SF-36, SUPPH
Tsay et al[24]	≥18 y old; have been receiving hemodialysis treatment for at least the last 6 mo; have no DSM IV psychiatric diagnoses; and have no major chronic illness	—	—	30	27	RCT	Outpatient dialysis units at 3 medical centers in northern Taiwan	Adaptation training program: needs assessment, cognitive behavior modification, problem-solving, and stress management	1/wk	120	8	Usual care	Degree of depression, quality of life, stress	BDI, SF-36
Krespi et al[18]	All the hemodialysis patients during the study period	—	—	51	50	RCT	The hemodialysis ward of a university hospital and its 4 satellite units	Special place imagery: listen to the tape on hemodialysis	3–4/wk	25	6	No-treatment	Degree of depression, anxiety, quality of life	HADS, SF-36

BAI = Beck Anxiety Inventory, BDI = Beck Depression Inventory, CBT = cognitive behavioral therapy, DSM IV = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, ESRD = end-stage renal disease, HADS = Hospital Anxiety and Depression Scale, HD = hemodialysis, IDWG = interdialysis weight gain, MINI = Mini-International Neuropsychiatric Interview, PSQI = Pittsburgh Sleep Quality Index, RCT = randomized controlled trials, SCL90 = Symptom Checklist 90, SF-36 = the MOS 36-Item Short Form Health Survey, SUPPH = Strategies Used by People to Promote Health.

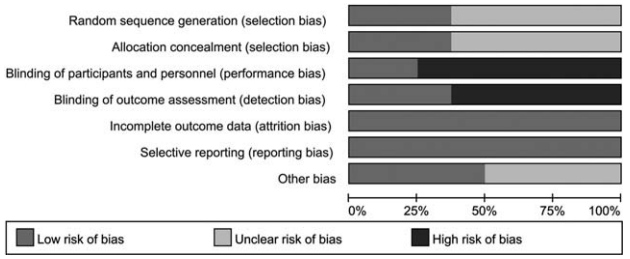

Figure 2. Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies.

random effects model. Therefore, we did not use the effect size but instead described only the results. Two studies reported the effectiveness of psychological interventions on hemodialysis patients' sleep quality ($P < 0.001$).

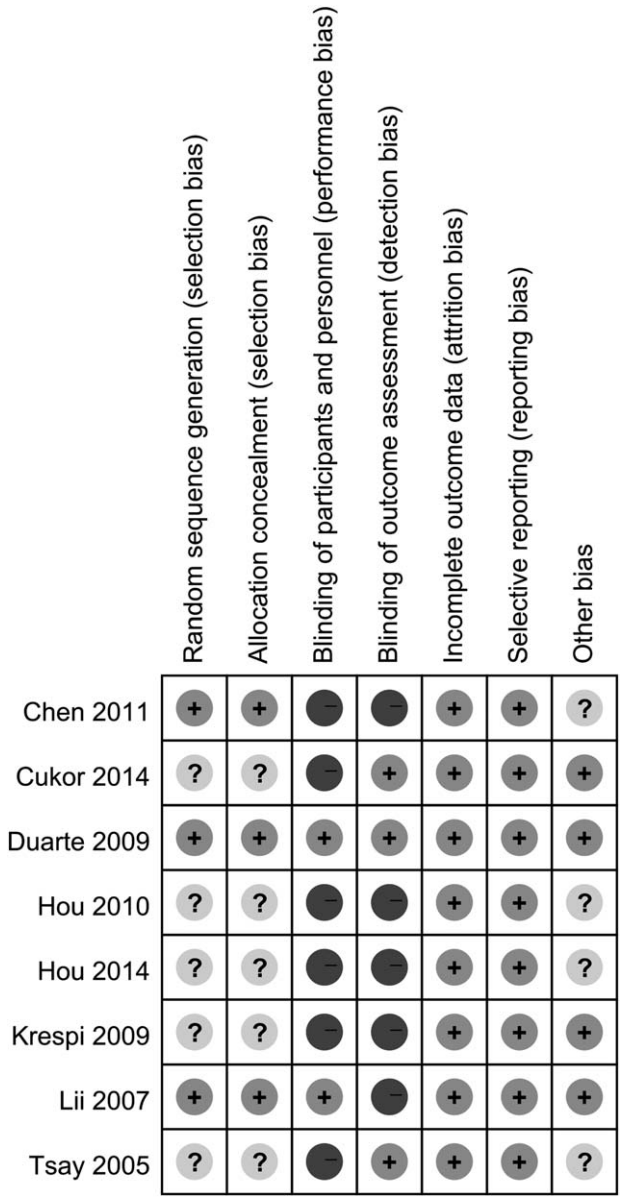

Figure 3. Risk of bias summary: review authors' judgments about each risk of bias item for each included study.

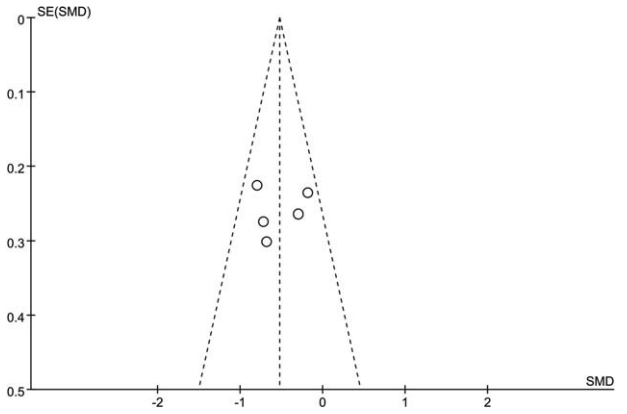

Figure 4. Funnel plot of comparison: psychological intervention versus control condition, outcome: degree of depression at post treatment. SE = standard error, SMD = standardized mean difference.

3.4.3. Fluid intake restriction adherence. We used IDWG to represent the fluid intake restriction adherence of hemodialysis patients. Two studies[20,26] involving 151 patients (81 in the intervention group and 70 in the control group) reported the effect of psychological interventions on hemodialysis patients' IDWG and showed statistically significant differences between the psychological intervention and the control (SMD −0.64, 95% CI: −0.96 to −0.31; $I^2 = 0\%$, $P = 0.35$), indicating that the fluid intake restriction adherence of hemodialysis patients may be improved by psychological interventions ($P < 0.001$) (Fig. 7).

3.4.4. Quality of life. Three studies[18,23,24] involving 206 patients (101 in the intervention group and 105 in the control group) reported the effect of psychological interventions on hemodialysis patients' quality of life. As shown in Fig. 8, there was no statistically significant difference between the psychological intervention and the control (SMD 0.40, 95% CI: −0.16 to 0.97, $P = 0.16$; $I^2 = 87\%$, $P < 0.001$), and the degree of heterogeneity was high. Because SF-36 can be divided into PCS and MCS, we used subgroup analysis to check whether psychological interventions can improve physical or mental quality of life. However, we found that there was still no statistically significant difference between the 2 groups (SMD 0.08, 95% CI: −0.48 to 0.64, $P = 0.78$; $I^2 = 74\%$, $P = 0.02$; SMD 0.72, 95% CI: −0.07 to 1.51, $P = 0.07$; $I^2 = 86\%$, $P < 0.001$). Therefore, regardless of the total, physical or mental quality of life, psychological interventions were not able to improve hemodialysis patients' quality of life. Moreover, the degree of heterogeneity was still high after adopting the random effects model, so we did not combine the data but instead only described it. Lii et al[23] and Tsay et al[24] found that quality of life was significantly improved statistically for hemodialysis patients by CBT and ATP ($P = 0.23$, $P = 0.97$; $P = 0.02$, $P = 0.001$), but Krespi's trial[18] showed that a specific imagery intervention did not have an effect on quality of life.

3.5. Quality of evidence

GRADE 3.6.1 was used to evaluate the quality of evidence. As shown in Table 2, outcomes of the degree of depression and IDWG were graded as moderate evidence, and the evidence grade of sleep quality was low. Because the same studies included assessment of the total, physical, and mental quality of life, they were graded as very low.

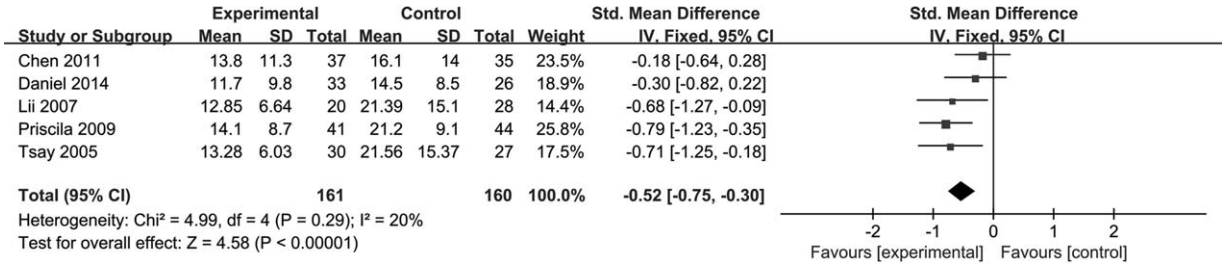

Figure 5. Forest plot of comparison: psychological intervention versus control condition, outcome: Standardized mean difference for the degree of depression at posttreatment. CI = confidence interval, SD = standard deviation.

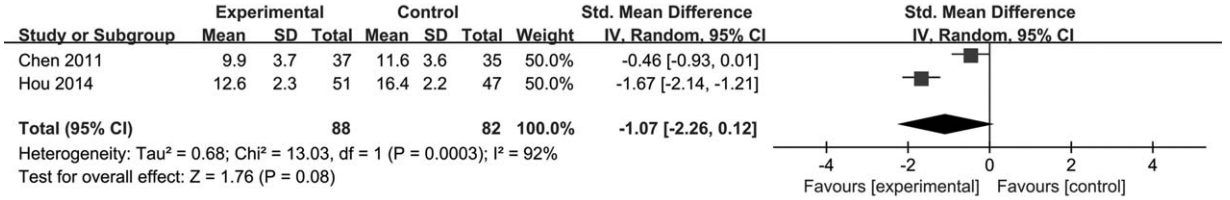

Figure 6. Forest plot of comparison: psychological intervention versus control condition, outcome: standardized mean difference for the sleep quality at posttreatment. CI = confidence interval, SD = standard deviation.

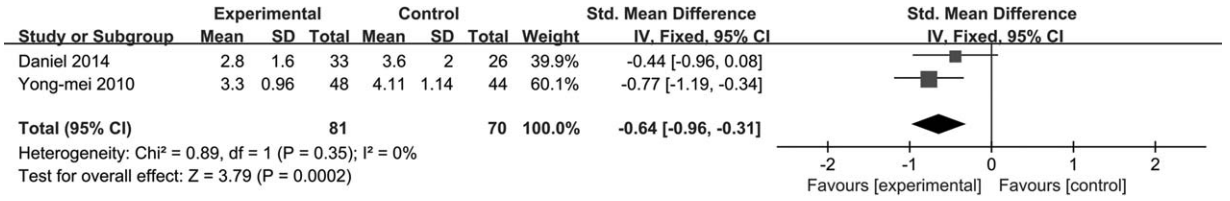

Figure 7. Forest plot of comparison: psychological intervention versus control condition, outcome: standardized mean difference for IDWG at posttreatment. CI = confidence interval, SD = standard deviation.

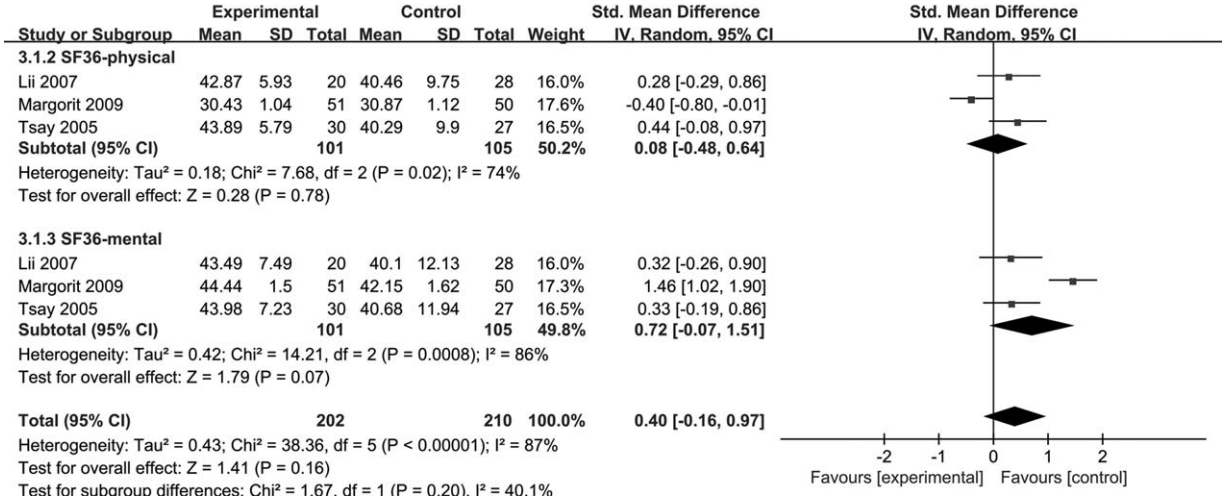

Figure 8. Forest plot of comparison: psychological intervention versus control condition, outcome: standardized mean difference for quality of life at posttreatment. CI = confidence interval, SD = standard deviation.

Table 2

Quality of evidence of included studies.

Variables / Outcomes	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Quality of evidence
Degree of depression	Serious (−1)	No	No	No	Undetected	Moderate
Sleep quality	Serious (−1)	Serious (−1)	No	No	Undetected	Low
IDWG	Serious (−1)	No	No	No	Undetected	Moderate
Quality of life	Serious (−1)	Serious (−1)	No	Serious (−1)	Undetected	Very low
PCS	Serious (−1)	Serious (−1)	No	Serious (−1)	Undetected	Very low
MCS	Serious (−1)	Serious (−1)	No	Serious (−1)	Undetected	Very low

IDWG = interdialysis weight gain, MCS = Mental Component Summary, PCS = Physical Component Summary.

4. Discussion

4.1. Summary of results

This study is the first meta-analysis of the effectiveness of psychological interventions on depression in hemodialysis patients. This meta-analysis provides evidence for doctors and nurses to potentially ameliorate depression via psychological interventions with these patients. All subjects in the included studies were hemodialysis patients. This approach can reduce the heterogeneity among studies but also restricts generalization in patients receiving other methods of dialysis. In addition to using depression as a primary outcome, we defined some outcomes related to depression as secondary outcomes, such as sleep quality, fluid intake restriction adherence, and quality of life, which made our meta-analysis more comprehensive. However, due to the methodological limitations of the included studies and the subjectivity of the assessment scales used, we failed to obtain any high-quality evidence in the present meta-analysis as the accumulated evidence ranged from very low to moderate quality.

4.1.1. Primary outcome. With the extensive application of holistic nursing, mental health has received increasing attention from nurses and has become an active research field. Extensive literature has reported the mental status of hemodialysis patients. The morbidity of depression in hemodialysis patients is extremely high. In Mollahadi et al's study[17] of psychological problems among hemodialysis patients, 6.5% of hemodialysis patients experienced depression. It is therefore important to reduce the symptoms of depression. Currently, antidepressants are still the main therapy for depression. NICE recommends treatment for at least 6 months and for at least 2 years if patients have a risk of relapse.[13] Many patients cannot maintain drug therapy because of its chronicity and side effects, such as drowsiness, dry mouth, tachycardia, and dependence.[14] As a complementary therapy, psychological interventions do not have the side effects of antidepressants and are easily accepted by patients. In our meta-analysis, psychological interventions affected the degree of depression of hemodialysis patients (MD = −5.73, $Z = 4.97$, $P < 0.001$). Our study is the first to reach this conclusion. All included studies used CBT as an intervention and BDI as a measurement to assess depression, which reduced heterogeneity to some extent. However, this scale is subjective, and we must interpret this result with caution. In addition, due to the nature of psychological interventions, it is difficult to blind participants and therapists, and few of the included studies described allocation concealment, resulting in some heterogeneity. For instance, Chen et al[21] used neither allocation concealment nor blinding, Cukor et al[20] did not blind the participants or the therapists, and Lii et al[23] did not blind the outcome assessors.

4.1.2. Secondary outcome. Depression in hemodialysis patients is likely to disturb sleep and reduce fluid intake restriction adherence, leading to low quality of life.[5,7,11] Therefore, determining whether psychological interventions can improve hemodialysis patients' sleep quality, fluid intake restriction adherence, and quality of life was another aim of this study.

The combined results revealed that psychological interventions were able to significantly improve hemodialysis patients' fluid intake restriction adherence (SMD = −0.64, $Z = 3.79$, $P < 0.001$). However, this result should be interpreted with caution because the 2 included studies did not use blinding and used different measurements of IDWG.

With regard to sleep quality and quality of life, the combined results showed no statistically significant differences between the intervention and control groups ($P = 0.08$; $P = 0.16$) regardless of whether subgroup analysis was used. This result differed from Yang et al's[30] results. In the review by Yang et al, there was significant improvement in the nonpharmacological intervention groups in comparison to the control group. Moreover, the heterogeneity of both sleep quality and quality of life were high after adopting the random effects model, so we did not combine the data and only described the results. Regarding sleep quality, the fact that the 2 studies did not blind the participants, personnel, and outcome assessment may have induced performance bias and detection bias. In addition, their duration of intervention, measurement time, and control groups differed. Moreover, the PSQI provides a subjective assessment of sleep quality. Regarding quality of life, the reason for the lack of statistically significant differences between the intervention and control groups may be as follows. First, the 3 included studies did not use the blinding of participants and personnel or the blinding of outcome assessment. Second, the psychological interventions used in these 3 studies differed; for example, Krespi[18] used no-treatment as the control group, which was different from the other 2 studies (usual care), and they obtained different results regarding the interventions (1 negative, 2 positive). Third, SF-36 is a subjective scale, and all the studies allowed patients to complete the scale independently, which may have resulted in large differences.

The included studies also reported the effectiveness of psychological interventions on hemodialysis patients' anxiety,[18,21] stress,[24] and self-efficacy.[23] However, due to the large differences between the assessment measures and the limited number of studies, we did not identify the effectiveness of psychological interventions on hemodialysis patients' anxiety as outcomes in this review to avoid unreliable conclusions.

4.2. Comparison with other published reviews

We retrieved only 1 meta-analysis published in the Cochrane Library in 2005 that studied the effects of psychological

interventions on hemodialysis patients' depression.[31] However, no RCTs were identified in their review. By comparison, all the RCTs retrieved that met the inclusion criteria were included in our review. We included depression as well as sleep quality, fluid intake restriction adherence, and quality of life as outcomes.

4.3. Implications for nursing practice

In hemodialysis patients, psychological interventions may reduce the degree of depression and improve fluid intake restriction adherence. However, due to high heterogeneity, effect size combinations of sleep quality and quality of life were not performed. Therefore, the current meta-analysis provides initial support for the practicability and effectiveness of psychological interventions because of the positive outcomes.

However, there are various types of psychological interventions, and some interventions are difficult to implement because of their long duration or complex content, leading to many drop outs in the majority of the included studies. To improve the adherence of patients receiving psychological interventions, nurses must adopt the best intervention in terms of the characteristics of the patients and the culture of the society. In addition, more convenient and easier methods of psychological interventions should be developed; for example, nurses can teach and guide patients through the Internet and can develop more efficient formats to shorten the duration of interventions.

4.4. Implications for future research

Because of the flaws in the original studies, such as low methodological quality, differences among all types of interventions and subjects, and the subjectivity of the questionnaires used, there was high heterogeneity among the studies and some bias. Hence, we could not draw conclusions based on high-quality evidence. The influence of psychological interventions on hemodialysis patients' depression remains to be further investigated by more rigorous studies. In this meta-analysis, we did not define pharmacotherapy as a control; thus, the relative effects of antidepressant and psychological interventions on hemodialysis patients' depression remain to be investigated. Because antidepressants are a mainstream therapy for depression, further investigations are necessary. If psychological interventions are more efficacious than antidepressants in ameliorating depression in hemodialysis patients, do not have the side effects of drugs, and are not expensive, then psychological interventions may be more widely used clinically and may reduce the burden on patients and medical systems. In addition, only a few studies included follow-ups in their investigations, so we could not evaluate the long-term effects of psychological interventions on the treatment of depression in hemodialysis patients. Thus, additional studies are recommended. Furthermore, the effects of other psychological interventions, such as MBCT (music therapy and mindfulness-based cognitive therapy), on depression in hemodialysis patients remain to be studied. To draw more reliable conclusions, the inclusion of certain types of psychological interventions or the use of subgroup analysis to evaluate the efficacy of each intervention is recommended. Finally, researchers should design more theoretically based and reliable implementation methods for psychological interventions.

4.5. Strengths and limitations

To the authors' knowledge, this meta-analysis is the first evidence-based study that includes all randomized controlled trials to evaluate the effect of psychological interventions on depression in hemodialysis patients. Moreover, we evaluated outcomes related to depression, such as sleep quality, fluid intake restriction adherence, and quality of life. The results are highly relevant to the daily work of doctors and have substantial clinical significance. With the exception of IDWG, the outcomes used the same evaluation measures: depression used BDI, sleep quality used PSQI, and quality of life used SF-36. All measures were divided into physical and mental parts, which may increase the homogeneity among studies. Finally, all the included studies used randomization, described drop outs, and compared baseline information for the 2 groups, which reduced some heterogeneity. It is worth mentioning that we included studies with negative results, which may help prevent some publication bias.

Nevertheless, several potential limitations should be discussed. First, the research methods of the studies were quite different. The included studies used several types of psychological interventions with a variety of characteristics according to actual conditions. However, the inclusion criteria of the subjects and the diagnostic criteria for depression varied according to the research objectives. These differences may result in a lack of comparability among studies, which may produce some bias. Second, most of the outcomes had strong subjectivity. With the exception of the IDWG, the outcomes used self-administered questionnaires as evaluation criteria, so the reliability needs to be further considered. Third, some data were incomplete, such as the criteria for depression and the duration of interventions. The lack of complete data makes it difficult for us to judge the reliability and comparability of the combined results. Fourth, none of the included studies reported the side effects of psychological interventions, so we could not conclude that psychological interventions were safe for hemodialysis patients. Fifth, the blinding of participants and assessors was not performed in many of the included studies, and few of the studies clearly described the allocation concealment and randomization, which may have led to a relatively low methodological quality. Thus, we were unable to draw high-quality conclusions about the effects of psychological interventions on hemodialysis patients' depression. Finally, our meta-analysis may not accurately evaluate publication bias because of the limited number of studies.

5. Conclusions

This meta-analysis is the first evidence-based study that includes all randomized controlled trials to evaluate the effects of psychological interventions on depression and related outcomes in hemodialysis patients. It demonstrated that psychological interventions may reduce the degree of depression and improve fluid intake restriction adherence. However, due to the high heterogeneity, effect size combinations of sleep quality and quality of life were not performed. The results have substantial clinical significance because they are highly relevant to the daily work of doctors and provide a more acceptable and comfortable method to reduce depression in hemodialysis patients. However, because most of the scales used to measure the outcomes had strong subjectivity, the methodological quality of some included studies was not very high, and none of the included studies reported the side effects of psychological interventions. We should thus interpret these results with caution. More rigorously designed and comprehensive research is needed.

Acknowledgments

The authors thank Professor Xiaolin Li (mental health center of West China Hospital, Sichuan University) for her assistance and guidance in designing and revising this manuscript. We appreciate the advice on statistical methods provided by Professor Guanjian Liu (a statistician from the West China Hospital, Sichuan University).

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