

간호사 주도의 중재가 신장이식 수혜자의 삶의 질, 약물 순응도, 불안 및 우울에 미치는 효과: 체계적 문헌고찰 및 메타분석

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The effectiveness of nurse-led interventions on quality of life, medication adherence, anxiety, and depression in kidney transplant recipients: A systematic review and meta-analysis

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Purpose: This study was conducted to evaluate the effects of nurse-led interventions on quality of life, medication adherence, anxiety, and depression in kidney transplant recipients. Methods: A systematic literature review was conducted following Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines. Two researchers independently selected the final literature, and the quality assessment was performed using Cochrane's Risk of Bias tool. Additionally, a meta-analysis was conducted using the statistical software RevMan 5.4 to estimate effect sizes. Results: Among the reviewed 2,264 papers, 8 final papers, including 6 from the literature search and 2 from manual searches, were included in the analysis. The total number of participants included in the analysis was 477. Nurse-led interventions were found to be effective in improving quality of life (d=1.05) and reducing anxiety (d=-0.98) and depression (d=-1.25). Due to the heterogeneity of the measurement tools, the effect size for medication adherence could not be calculated. Despite this, nurse-led interventions were shown to improve medication adherence. In the cases of anxiety and depression, longer intervention periods showed a more significant reduction trend. Conclusion: The results of this study suggest that nurse-led interventions positively impact quality of life, medication adherence, anxiety, and depression in kidney transplant recipients. Therefore, it is important to recognize the crucial role of nurses and explore ways to provide continuous nursing interventions for kidney transplant recipients.

Keywords: Kidney, Medication adherence, Meta-analysis, Quality of life, Transplants

Introduction

Background

With the increase in the aging population occurring on a global

scale, the prevalence of metabolic syndrome and hypertension has also risen, leading to a higher number of chronic kidney disease (CKD) patients. In the United States, CKD affects 14% of the adult population, which equates to 35.5 million people, or one in seven adults [1]. In South Korea, the number of CKD patients

주요어: 신장, 약물 순응도, 메타분석, 삶의 질, 이식

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increased by over 30%, from 203,978 in 2017 to 277,252 in 2021 [2]. Kidney transplantation (KT), one of the renal replacement therapies for end-stage renal disease (ESRD), has been known to offer higher survival rates compared to dialysis. In addition, after KT, ESRD patients experience relatively easier dietary management, increased physical activity, and a smoother return to day-to-day life, along with cost savings and reduced complications, making KT the most ideal treatment method [3]. Due to these advantages, the number of kidney transplant recipients increased from 1,760 in 2013 to 2,034 in 2022, and the number of patients waiting for a kidney transplant more than doubled from 14,181 in 2013 to 32,227 in 2022 [4].

However, immunosuppressants, which are essential for the success of kidney transplants, can cause infections, transplant rejection, increased malignancy, hypertension, diabetes, hyperlipidemia, cardiovascular diseases, muscle weakness, and osteoporosis due to steroid use, leading to various physical issues [5-7]. Early diagnosis and appropriate treatment of these physical complications are necessary after KT, as they negatively impact long-term survival rates and quality of life. Therefore, meticulous management and thorough monitoring of complications are required post-transplantation [6-8]. Additionally, psychological issues such as fear of rejection or death, anxiety, and depression can arise [9,10]. These psychological problems are associated with the potential for returning to a normal life, lack of information about the treatment process and complications, difficulty in making rational management decisions, and complications relating to knowledge, attitudes, and actions regarding disease management [10]. Therefore, post-transplant care must involve regular and continuous follow-up in various aspects, such as medication management, early detection of transplant rejection, prevention of complications and infections, dietary and day-to-day management, and psychological counseling support [11,12].

Lack of information about post-transplant care can lead to non-adherence to treatment instructions, such as irregular intake of immunosuppressants, which affects potential health outcomes and quality of life [5,13,14]. Conversely, nurse-led education and monitoring for kidney transplant recipients have been shown to improve behavioral changes, enhance quality of life, and alleviate psychological states such as anxiety and depression [1,15,16]. Furthermore, interventions such as home visits by nurses for education and counseling have been effective in improving medication adherence among kidney transplant recipients [9]. Therefore, continuous intervention is needed for kidney transplant

recipients to enhance adherence to treatment instructions both during hospitalization and after discharge. In addition, various intervention strategies need to be researched.

Literature reviews on kidney transplant recipients have primarily focused on types of interventions such as exercise, education, counseling, and financial support [17,18], or methods of delivering interventions like computers and smartphones [19]. However, there has been no review based on the characteristics of the intervention providers. Nurses, who frequently interact with patients and can deliver individualized interventions reflecting the patients' characteristics and needs, play a crucial role in providing education both before and after KT, preparing patients physically and mentally for surgery, administrating medications, implementing post-operative wound care, monitoring patients for complications, and managing diet and exercise [20,21]. Additionally, nurses play a significant role in multidisciplinary teams by providing direct care, information, and emotional support to reduce patients' anxiety [22].

Despite the expanding role of nurses alongside the increasing number of kidney transplant recipients, there is still a lack of evidence on the effectiveness of nurse-led interventions. Therefore, it will be necessary to systematically review studies on nurse-led interventions for kidney transplant recipients, integrate the results of studies with various characteristics, and calculate an effect size to draw objective conclusions through meta-analysis. This study aims to closely analyze the effectiveness of nurse-led interventions for kidney transplant recipients and provide a direction for planning and operating effective, evidence-based nurse-led interventions.

Research objectives

The purpose of this study is to systematically review randomized controlled trial (RCT) papers that have examined the effects of nurse-led interventions on kidney transplant recipients, and to conduct a meta-analysis to estimate the effect size. The specific objectives are as follows:

- To assess the effect of nurse-led interventions on the quality of life of kidney transplant recipients.
- To evaluate the effect of nurse-led interventions on medication adherence among kidney transplant recipients.
- To determine the effect of nurse-led interventions on anxiety and depression among kidney transplant recipients.

Methods

Design

This study is a systematic review and meta-analysis of RCTs that analyzed the impact of nurse-led interventions on quality of life, medication adherence, anxiety and depression and among kidney transplant recipients. The methodology of this study is outlined in the protocol registered with PROSPERO (PROSPERO registration: CRD42024545382).

Key question

The key question of this study is: "Are nurse-led interventions effective in improving quality of life among kidney transplant recipients?"

Criteria for data selection

This study was conducted in accordance with the guidelines for systematic reviews and meta-analyses (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [23]. The criteria for selecting the analyzed papers are as follows:

Participants

This study targeted kidney transplant recipients aged 18 and older. Papers involving participants who received simultaneous transplantation of kidneys and other organs were excluded.

Interventions

The study focused on nurse-led interventions conducted with kidney transplant recipients.

Comparisons

The comparison group consisted of kidney transplant recipients who did not receive nurse-led interventions, including those who received usual care or were only provided with educational booklets.

Outcomes

Selected papers provided measurements of quality of life, medication adherence, anxiety, and depression after nurse-led interventions.

• Study types

This study included only RCTs where nurses directly administered the interventions. Non-RCTs, observational studies, qualitative studies, and protocols were excluded.

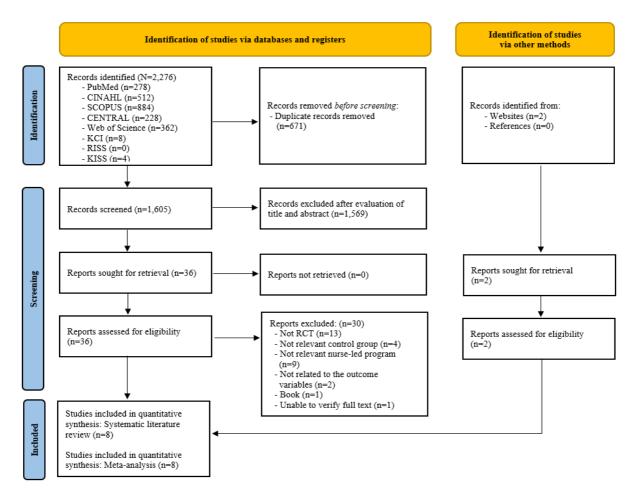
Literature search and selection

• Data search

Data search and collection were conducted from October 20 to October 25, 2023, focusing on domestic and international literature published up to October 2023. The international databases used were PubMed, CINAHL, SCOPUS, CENTRAL, and Web of Science, while the domestic databases included RISS, KISS, and KCI. Additionally, online searches were conducted using these databases, and reference lists were manually checked. The search strategy applied appropriate combinations of MeSH terms, text words in titles and abstracts, and truncation using AND/OR. For international papers, the search terms used were ("kidney transplantation" [MeSH] OR "kidney transplant*" OR "renal transplant*") AND (education [MeSH] OR education* OR intervention* OR program* OR care*) AND (nursing OR "nurse-led"). For domestic papers, the search terms were '신장이 식' AND '간호' AND ('중재' OR '교육' OR '프로그램'). The publication year was not restricted, and the search was limited to studies published in English and Korean. Retrieved papers were collected and organized using EndNote 21 (Clarivate Analytics) and Excel 2016 (Microsoft).

• Data selection and extraction

Duplicate records were removed using EndNote, and two researchers independently reviewed the titles, abstracts, and full texts of the retrieved papers. During this process, the researchers recorded the reasons for excluding certain papers. If there was a disagreement between the researchers, they reviewed the study together to reach a consensus. If no agreement was reached even after the research meeting, the final selection was made in consultation with a nursing professor who was not involved in the study. The literature search resulted in a total of 2,276 papers, including 12 domestic and 2,264 international studies. After removing duplicates, 671 papers were excluded, leaving 1,605 titles and abstracts to be reviewed. This resulted in the initial selection of 36 papers. Upon further review of the full texts, the following exclusions were made: 13 non-RCT studies, 4 studies where the control group received only routine care or educational



RCT=randomized controlled trial

Figure 1. Flow chart showing study selection

booklets, 9 studies where the intervention was not nurse-led, 2 studies that did not measure quality of life, medication adherence, anxiety, or depression, 1 book, and 1 study where the full text could not be accessed. In total, 6 studies were selected, with an additional 2 studies identified through manual search, resulting in a final selection of 8 studies (Figure 1).

• Quality assessment of the literature

The quality of the selected papers was assessed using Cochrane's Risk of Bias 1.0 tool, as recommended by Cochrane Collaboration's guidelines for systematic reviews. Two researchers independently conducted the assessments, and any disagreements were resolved by re-examining the original papers before reaching a consensus.

Data analysis

To analyze the characteristics of studies on nurse-led interventions for kidney transplant recipients, the following information was examined: the author, publication year, country of study, study design, number and average age of participants, intervention methods (name, content, duration), outcome measurement tools, and study results. For the quantitative synthesis of selected literature, the effect size of the interventions was calculated using Cochrane Library's RevMan 5.4 program. Meta-analysis was performed when there were identical outcome variables available for analysis or when pre- and post-intervention quantitative values for outcome variables were provided. Due to the small number of synthesized studies, which made it impossible

to estimate between-study variance, a fixed effect model was used for calculation.

The outcome variables of the synthesized studies were continuous, and the effect size was analyzed using standard deviation. Given the use of various measurement tools across studies, the standardized mean difference was calculated. The effect and 95% confidence interval (CI) for each outcome variable were analyzed using inverse variance. Heterogeneity among studies was assessed using forest plots to check the direction of effect sizes and overlapping CIs among individual studies. Statistical tests for heterogeneity were evaluated using the I2- and Q-values. An I²-value of 25% or less indicated low heterogeneity, a value of around 50% indicated moderate heterogeneity, and a value of 75% or more indicated high heterogeneity. A Q-value with a significance level of <.05 was considered to indicate heterogeneity. Subgroup analysis was performed according to the measurement timing of the outcomes. Publication bias was not assessed due to the requirement of at least 10 studies.

Ethical considerations

This study was conducted using previously published papers and received an exemption from review by the Institutional Review Board of Jeonbuk University (IRB No. JBNU 2024-05-016).

Results

Data selection

A total of 2,276 papers were retrieved from domestic and international databases. Using EndNote, 671 duplicate papers were removed. Subsequently, based on the selection and exclusion criteria, two researchers independently reviewed the titles and abstracts, resulting in the exclusion of 1,605 papers. This initial screening led to the selection of 36 studies. These 36 papers were further reviewed in full text according to the same criteria, leading to the exclusion of 30 papers. Therefore, six papers were selected, and an additional two papers were identified through manual searching, resulting in a final selection of eight papers (Figure 1; Appendix 1).

Characteristics of included studies

The characteristics of the eight studies on nurse-led interventions included in this systematic review are as follows (Table 1). In terms of the distribution by year of study, one study (12.5%) was conducted before 2010, three studies (37.5%) were conducted between 2010 and 2019, and four studies (50.0%) were conducted after 2020, indicating a steady publication of related research. The countries of study were Iran (3 studies, 37.5%), China (3 studies, 37.5%), the United States (1 study, 12.5%), and Switzerland (1 study, 12.5%). No domestic studies were identified. All studies were RCTs, including 2 pilot RCTs and 1 multi-center RCT.

Participants

The total number of participants in the included studies was 477 (239 in the intervention group and 238 in the control group). The participants were kidney transplant recipients aged 18 and older, with an average age of 42.9 years, and 65.8% were male.

Interventions

The nurse-led interventions for kidney transplant recipients included in the systematic review consisted of educational interventions in seven studies (87.5%) and physical exercise training in one study (12.5%). Seven studies (87.5%) implemented continuous interventions in both medical institutions and at home, while one study (12.5%) provided interventions only during hospitalization post-surgery. Among the seven studies providing educational interventions, six had intervention durations ranging from a minimum of three weeks to a maximum of six months, while one study did not specify a duration but provided additional interventions before surgery, seven days post-surgery, and before discharge. The study offering exercise interventions provided them from three days post-surgery for a duration of three months.

The specific types of educational interventions included two studies based on the Continuous Care Model; one study providing education on medication, diet, and self-care enhancement; one study aimed at improving self-efficacy; one study using the Health Belief Model to elicit positive behavioral changes in kidney transplant recipients; one study focused on identifying and solving problems experienced by recipients post-transplant; and one study based on the plan-do-check-act cycle to enhance self-improvement through continuous management. All studies used a mix of delivery methods for education, such as regular home visits, face-to-face education during outpatient visits, telephone calls, and booklets. In addition, the educators also acted as follow-up

Table 1. Characteristics of the Included Studies

-	Study duration	weeks	3 months	3 months	Before discharge
	Findings	• QoL (+) 6	• Medication adherence (+) 3 • Attrition rate: 27.8%	• Nursing satisfaction (+) • Drug compliance (+) • QoL (+) • Anxiety and depression (-) • Self-management ability (+)	• Anxiety and depression (-) B. • Physiological function (+) di • QoL (+) • Attrition rate: 5.6%
-	Outcome measurement	• Quality of life (KTQ-25)	• Medication adherence (level)	Anxiety (SAS) Depression (SDS) Quality of life (Quality of Life Scale) Medication compliance (Basel assessment scale) Self perceived burden (SPBS) Self-management ability Nursing Satisfaction	• Anxiety and depression (HADS)
	Control	Usual care	Usual care	Usual care	Usual care
	Intervention	Self-care education program Sessions of 30 to 45 minutes every other day Step 1: a description of the research, face-to-face interview Sep 2: three training sessions Step 3: encounters at the department of nephrology ontents: nature of the disease, its etiology, clinical symptoms, diagnosis, treatment, and complications/principles of medication administration and side effects/diet regimen and physical and self-care activities Individual intervention	Supporting medication adherence in renal transplantation (SMART) Three follow-up calls, once a month for three months Step 1: enhanced routine care plus one home visit Step 2: telephone follow-up Step 3: EM monitoring follow-up Contents: medication taking, medication management, reasoning for failing to take the medication (discussed the EM printout) Individual intervention/Social support interventions	Nursing intervention based on health belief model - 3 sessions of 30 to 45 minutes every other day - 1 onth: provide with the drug-taking manual, fill in the medication plan and schedule 2 months: keep the blood concentration stable, rejection occurrence, treatment of infection 3 months: prevention and treatment of complications, prevention and treatment of complications, self-monitoring indicators - Fo ow-up the patients by phone/WeChat/SMS semimonthly - Individual intervention	• Nursing intervention based on a solution-focused approach (SFA) - 5 terventions in total for 30–60 minutes - St 1: describing the problem, developing well-formed goals, exploring for exceptions, end of session feedback, and evaluating progress (five stages) Step 2: follow-up at 1, 3, and 6 months after surgery • Individual intervention
	O E	30	12	30	46
ants	a (c)	5 29	9 9	7 30	4 37
Participants	Male (%)	69.5	78.6	56.7	63.4
4	Age (mean)	Exp: 42.72 Cont: 41.5	45.6	Exp: 45.91 Cont: 45.96	Exp: 38.32 Cont: 40.97
	Design	RCT	RCT	RCT	RCT
	Country	Iran	Switzerland Pilot	China	China
-	Author (year)	Aghakhani Iran et al. (2021)	De Geest et al. (2006)	(2022)	(2023)

Table 1. Characteristics of the Included Studies (Continued)

, -		•	Par	Participants	S						70.40
(year)	Country Design	Design	Age (mean)	Male (%)	ШΞ	U E	Intervention	Control	measurement	Findings	duration
Raiesifar et al. (2014)	Iran	Multi-cen 37.5 ter RCT	37.5	73.1	41	37 •	 Continuous care model St 1: familiarization and sensitization of patients towards the disease (30 minutes) Step 2: self-management programs using lectures, question-and-answer, counseling, and educational booklets (2 to 3 hours) Step 3: model compliance and continuous follow-up, repeated phone calls and regular visits Individual intervention 	Usual care	• Quality of life (KTQ-25)	• At 1 and 3 months, QoL scores (+) • At 2 months, fatigue, fear, and emotional insecurity (+) • Attrition rate: 13.3%	3 months
Russell et al. (2011)	USA	Pilot RCT	51.5	44	∞	_	Continuous self-improvement intervention (plan-do-check-act process) St 1: provided with educational brochures developed by the international transplant (home visit, mailed) Step 2: monthly telephone calls Individual intervention	Provided with educational brochure	Medication adherence (Medication Event Monitoring System [MEMS])	• Medication adherence (+)	6 months
al. (2015)	Iran	RCT	48.19	61.4	35	35 •	 Continuous care model 3 sessions of 30 to 45 minutes every other day St 1: familiarizing (30-45 minutes) Step 2: making sensitive; counseling sessions, group discussion, speech, question and answer, and individual sessions (1~2 hours) Step 3: controlling; patient tracking and control over the phone (3 months) Step 4: appraising; evaluation the follow-up Individual intervention/social support interventions 	Usual care	• Depression, anxiety, and stress (DASS-21)	• Depression, anxiety, and stress (-) • Attrition rate: 12.5%	3 months
Zhang et al. (2023)	China	RCT	Exp: 43.16 Cont: 42.06	76.9	23		A nurse-led standard physical exercise program St 1: daily exercise rehabilitation video and sent the video to the nurses by smartphone Step 2: general health consultations and outpatient follow-up reminders by telephone Individual intervention	Usual care	Anxiety (SAS) Depression (SDS) Quality of life (SF-36) Fatigue (MFI-20) Sport motivation (SMS) Clinical characteristics (heart rate, BMI, blood glucose, creatinine, and triglyceride level) Body composition measurements (InBody S10) 6-MWT, 30s-CST	• Anxiety, depression, and fatigue (-) • Sport motivation (+) • Body composition measurements (+) • 6-MWT and 30s-CST (+) • Attrition rate: 1.8%	3 months

(-)=experimental group significantly decreased; (+)=experimental group significantly improved; 30s-CST=30-second chair stand test; 6-MWT=6-minute walk test; BMI=body mass index; C=control group; Cont=control group; DASS-21=short-from version of the depression, anxiety, and stress scales; E=experimental group; EM=electronic monitoring; Exp=experimental control group; DASS-21=short-from version of the depression, anxiety, and stress scales; E=experimental group; EM=electronic monitoring; Exp=experimental control group; DASS-21=short-from version of the depression, anxiety, and stress scales; E=experimental group; EM=electronic monitoring; Exp=experimental group; EM=electronic monitoring; E transplantation; RCT=randomized controlled trial; SAS=self-rating anxiety scale; SDS=self-rating depression scale; SF-36=36-Item short form health survey; SMS=sport motivation scale; group; KTQ-25=kidney transplant questionnaire-25-items; MFI-20=20-item multidimensional fatigue inventory; QoL=quality of life; QOL-RT=quality of life scale for patients of renal SPBS=self-perceived burden scale

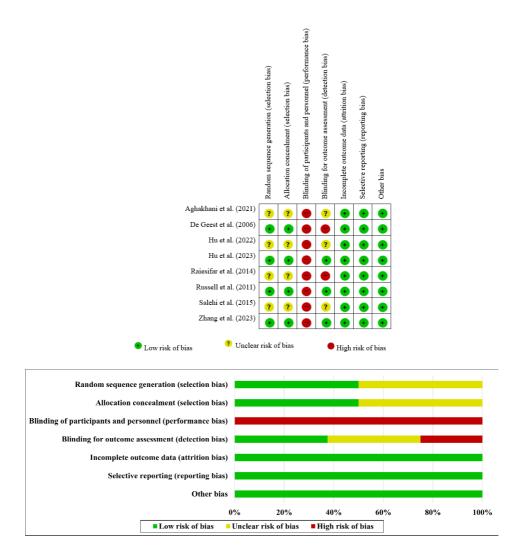


Figure 2. Risk of bias

observers.

Outcome Variables

Of the eight studies, five (62.5%) measured quality of life as an outcome variable, three (37.5%) reported on medication adherence, and four (50.0%) measured anxiety and depression. Tools used to measure quality of life included Kidney Transplant Questionnaire-25-items (2 studies), Quality of Life Scale for Patients of Renal Transplantation, 36-Item Short Form Health Survey, and the Quality of Life Scale. The Quality of Life Scale interpreted lower scores as indicating higher quality of life, which differed from other quality of life measurement tools. For consistency in statistical analysis, the mean values were converted to negative scores to align the directionality of results before

synthesis. Tools used to measure medication adherence included the medication adherence level, Basel Assessment Scale, and the Medication Event Monitoring System. Tools used to measure anxiety included Self-Rating Anxiety Scale (2 studies), Anxiety subscale of the Hospital Anxiety and Depression Scale, and short-from version of the Depression, Anxiety, and Stress Scales (DASS-21), while tools used to measure depression included Self-Rating Depression Scale (2 studies), Depression subscale of the Hospital Anxiety and Depression Scale, and DASS-21.

Results

Among the five studies measuring quality of life as the primary variable, four reported a significant improvement in quality of life compared to the control group. Four of these five studies applied long-term interventions of at least three weeks, while one study, although not specifying an exact intervention duration, conducted interventions from the day before the transplant to seven days post-surgery and provided additional interventions before discharge, suggesting a minimum duration of one week. All three studies measuring medication adherence as the primary variable applied long-term interventions of at least three months and reported an increase in medication adherence. All four studies measuring anxiety and depression applied long-term interventions and reported reductions in anxiety and depression.

Quality assessment of the literature

The quality assessment results of the eight final selected studies are shown in Figure 2. Among the evaluation items, random sequence generation was mentioned in four studies (50.0%), and allocation concealment was mentioned in four studies (50.0%), both of which were evaluated as low risk. However, blinding of outcome assessors was mentioned in only three studies (33.3%), indicating a high risk of bias. Blinding of participants and personnel showed a high risk of bias in all 8 studies (100%), primarily due to the nature of the interventions, which made blinding of participants difficult. Most of the studies included in this review applied a single-blind method. Incomplete outcome data, selective reporting, and other potential threats to validity were assessed as low risk across all studies.

Estimated effect size of nurse-led interventions

A total of eight studies were analyzed to estimate the effect size of nurse-led interventions on the quality of life, anxiety, and depression of kidney transplant recipients (Figure 3). Studies with medication adherence as a variable showed heterogeneity in measurement tools and did not present means and standard deviations for medication adherence, making meta-analysis unfeasible.

• Quality of life

Five studies measured quality of life as a primary variable, presenting means and standard deviations. All applied interventions lasted at least one week. One study reported integrated scores across all quality of life domains, two studies reported both integrated and subdomain scores (physical, psychological, social), and two studies reported only subdomain

scores. Meta-analysis was conducted separately for studies reporting integrated scores and those reporting subdomain scores.

For studies reporting integrated quality of life scores, three studies were analyzed. Subgroup analysis was conducted based on the measurement timing post-intervention: 1~2 months and 3~6 months. Quality of life measured 1~2 months post-intervention showed a significant improvement with an effect size of 1.58 (n=77, 95% CI 0.96~2.19, Z=5.02, p<.001). However, high heterogeneity was observed (x²=36.66, df=2, p<.001, I²=95%). Quality of life measured 3~6 months post-intervention also showed significant improvement with an effect size of 0.86 (n=130, 95% CI 0.49~1.23, Z=4.57, p<.001) and moderate to high heterogeneity (x²=11.16, df=3, p=.010, I²=73%; Figure 3-A).

For the physical domain of quality of life, four studies were analyzed, with subgroup analysis based on measurement timing: $1\sim3$ months and $4\sim6$ months. Quality of life in the physical domain showed a significant improvement with an effect size of 1.02 (n=125, 95% CI $0.61\sim1.44$, Z=4.85, p<.001) at $1\sim3$ months post-intervention, but with high heterogeneity ($x^2=36.08$, df=4, p<.001, $I^2=89\%$). Quality of life measured $4\sim6$ months post-intervention showed an effect size of 0.12 (n=189, 95% CI $-0.17\sim0.41$, Z=0.82, p=.410), which was not statistically significant and exhibited high heterogeneity ($x^2=13.30$, df=2, p<.001, $I^2=85\%$; Figure 3-B).

For the psychological domain of quality of life, four studies were analyzed. Subgroup analysis showed that at $1\sim3$ months post-intervention, the effect size was 0.22 (n=125, 95% CI -0.19 \sim 0.62, Z=1.04, p=.300), which was not statistically significant and had high heterogeneity (x^2 =52.59, df=4, p<.001, I^2 =92%). At 4 \sim 6 months post-intervention, the effect size was 0.08 (n=189, 95% CI -0.21 \sim 0.37, Z=0.53, p=.590), which also was not statistically significant, with moderate heterogeneity (x^2 =4.95, df=2, p=.080, I^2 =60%; Figure 3-C).

For the social domain of quality of life, three studies were analyzed. At $1\sim3$ months post-intervention, the effect size was 0.46 (n=48, 95% CI -0.11 \sim 1.04, Z=1.57, p=.120), showing no statistically significant improvement but with no heterogeneity (x^2 =0.13, df=1, p=.720, I 2 =0%). At 4 \sim 6 months post-intervention, the effect size was 0.29 (n=189, 95% CI -0.01 \sim 0.58, Z=1.91, p=.060), showing no statistically significant improvement and high heterogeneity (x^2 =20.69, df=2, p<.001, I 2 =90%; Figure 3-D).

Medication adherence

Three studies measured medication adherence as a primary

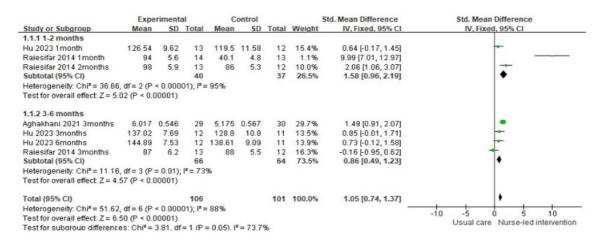


Figure 3-A. Quality of life

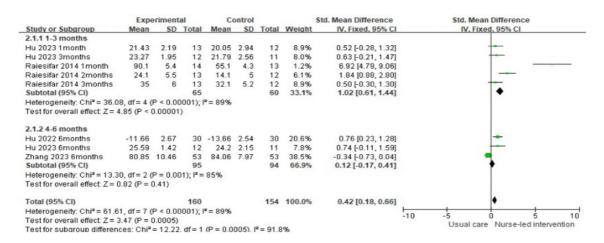


Figure 3-B. Physiological function of quality of life

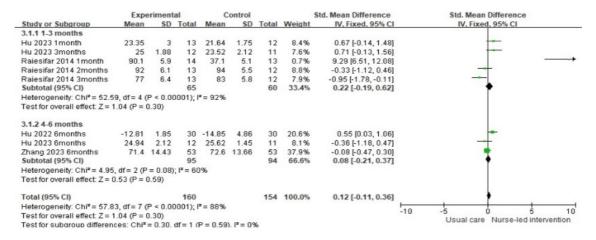


Figure 3-C. Psychological function of quality of life

Figure 3. Forest plot of meta-analysis on the effects of nurse-led interventions

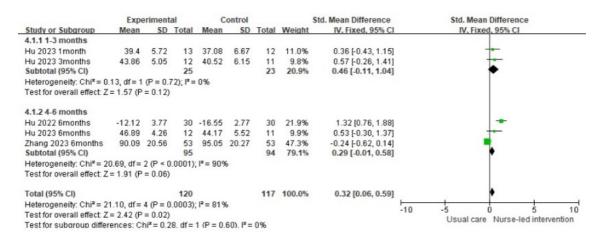


Figure 3-D. Social function of quality of life

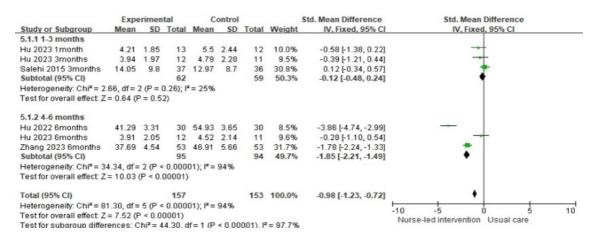


Figure 3-E. Anxiety

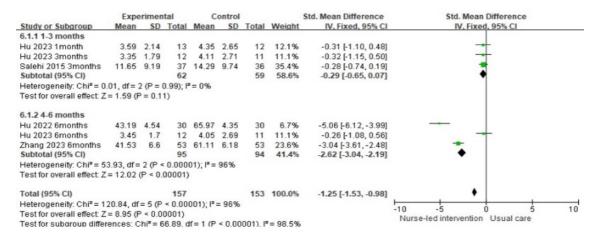


Figure 3-F. Depression

Figure 3. Forest plot of meta-analysis on the effects of nurse-led interventions (continued)

variable, focusing on kidney transplant recipients with low medication adherence. However, due to varying reporting formats, quantitative synthesis was not possible. Two studies measured adherence through the opening of electronic medication caps and bottles, while one study used a self-reported questionnaire to assess missed or taken medications. All three studies applied continuous home visits, phone calls, and printed educational materials over more than three months, resulting in increased medication adherence in the intervention group compared to the control group.

Anxiety

Four studies reported anxiety scores with means and standard deviations, comparing nurse-led interventions to usual care. All applied interventions lasted at least one week to a maximum of 12 weeks. Subgroup analysis based on measurement timing showed that at 1~3 months post-intervention, anxiety decreased with an effect size of -0.12 (n=121, 95% CI -0.48~0.24, Z=0.64, p=.520), which was not statistically significant and had low heterogeneity (x^2 =2.66, df=2, p=.260, I 2 =25%). At 4~6 months post-intervention, anxiety decreased with an effect size of -1.85 (n=189, 95% CI -2.21 to -1.49, Z=10.03, p<.001), which was statistically significant but had high heterogeneity (x^2 =34.34, df=2, p<.001, I 2 =94%; Figure 3-E).

Depression

Four studies reported depression scores. Subgroup analysis based on measurement timing showed that at $1\sim3$ months post-intervention, depression decreased with an effect size of -0.29 (n=121, 95% CI -0.65 \sim 0.07, Z=1.59, p=.110), which was not statistically significant and had no heterogeneity (x^2 =0.01, df=2, p=.990, I^2 =0%). At 4 \sim 6 months post-intervention, depression decreased with an effect size of -2.62 (n=189, 95% CI -3.04 to -2.19, Z=12.02, p<.001), which was statistically significant but had high heterogeneity (x^2 =53.93, df=2, p<.001, I^2 =96%; Figure 3-F).

Discussion

This study systematically reviewed nurse-led interventions to determine their effectiveness in improving quality of life, medication adherence, anxiety, and depression among kidney transplant recipients, including eight RCT studies. According to the evidence pyramid for evaluating the level of evidence, RCT

studies, aside from systematic reviews and meta-analyses, are at the top of the pyramid [24]. This indicates that results from RCT studies provide high-quality evidence that can be applied in practice. All eight RCT studies included in this research were conducted abroad, suggesting a need for efforts to conduct high-quality RCT studies in the domestic nursing field as well. The quality assessment of the eight included studies generally showed a low risk of bias, but due to the nature of the interventions, the risk of bias was high in blinding participants and outcome assessors. Among the analyzed studies, 87.5% (7 studies) were conducted after 2010, and 50.0% (4 studies) were published after 2020. This indicates a gradual increase in nurse-led interventions for kidney transplant recipients and highlights the need for such interventions.

Most nurse-led interventions consisted of educational programs (7 studies) and were implemented continuously, both in hospitals and at homes. Kidney transplant recipients often struggle to adapt to their new lives after receiving a kidney transplant [25], and they may feel fear and an increased burden when transitioning from receiving care from healthcare professionals in the hospital to self-managing at home [26]. Therefore, it may be effective to conduct continuous nursing interventions that do not distinguish between medical institutions and the community to help kidney transplant recipients adapt to their new situations.

Integrated quality of life scores were found to be higher in the nurse-led intervention group compared to the usual care group. When divided by measurement time, the difference between the intervention and control groups was greater when measured 1~2 months post-intervention compared to 3~6 months. Kidney transplant recipients generally experience improved quality of life as they gradually adapt to their new kidneys compared to life before the transplant when they were on hemodialysis or peritoneal dialysis [27]. Early intervention by nurses appears to accelerate the improvement in quality of life during the adaptation period to the new situation. In the subdomains of quality of life (physical, psychological, social), the nurse-led intervention group showed higher scores than the usual care group, with a greater difference observed at 1~3 months. The psychological domain showed the smallest effect size compared to the physical and social domains, aligning with findings from previous studies [28] that reported psychological issues are less likely to be addressed compared to other areas due to insufficient information and education from healthcare providers. Continuous provision of information and education by healthcare professionals, along with counseling to address individual psychological issues, is necessary.

Three studies that confirmed medication adherence had diverse measurement tools and outcomes, making quantitative synthesis impossible. All three studies targeted kidney transplant recipients with low medication adherence and reported improved adherence. Kidney transplant recipients are reported to have lower medication adherence compared to other organ transplant recipients [29-31], which increases the risk of transplant failure and reduces patients' expected lifespan [32]. Factors influencing medication adherence include personal characteristics such as age, gender, and education level, as well as psychological factors such as self-efficacy, treatment beliefs, stress, and the complexity and duration of the treatment process [33]. Therefore, it will be necessary to establish and provide individualized, multidimensional nursing interventions considering the recipients' circumstances. According to previous studies, medication adherence was better maintained in the group that received both reminders from the electronic monitoring (EM) device and notifications from providers compared to the group that received only reminders from the EM device [34]. Nurses, who have the most frequent contact with kidney transplant recipients, provide interventions that consider the individual's specific needs. In multidisciplinary team care, nurses are well-suited to determine the most appropriate personalized interventions for individuals, provide education to recipients, and perform various interventions such as long-term tracking of medication adherence. Therefore, nurses are considered the most suitable providers for this role [35]. Additionally, all three studies applied long-term interventions of more than three months, resulting in increased medication adherence. Kidney transplant recipients face drastic changes before and after surgery, resulting in extreme stress, where brief, one-time education is not effective for knowledge acquisition or comprehension [36]. This aligns with previous studies [17], which found that long-term interventions of more than three months were more effective in increasing medication adherence than one-time interventions. Therefore, it is essential to develop systematically structured nursing strategies to provide long-term, continuous care to enhance medication adherence among kidney transplant recipients.

Four studies measured anxiety and depression, showing greater reductions at 4-6 months post-intervention compared to 1-3 months. Between 20%-60% of kidney transplant recipients experience anxiety and depression [37], which negatively impact self-management abilities such as diet and physical activity, as well as hematological components such as endogenous creatinine

clearance [38]. Additionally, these psychological disorders negatively affect medication adherence, increasing the risk of transplant complications or rejection, ultimately lowering the quality of life [39,40]. The results of this study are consistent with previous research [9,15] that found continuous education and monitoring by nurses play a crucial role in alleviating the psychological state of kidney transplant recipients. Moreover, recipients of solid organ transplants who receive psychotherapy before and after transplantation demonstrated improved treatment adherence and reduced anxiety and depression [41,42]. However, to address drawbacks such as reluctance to participate in interventions and skepticism about their effectiveness, it is necessary to provide regular and appropriate interventions by healthcare providers to assess psychological disorders such as anxiety and depression [42]. Therefore, it will be necessary for nurses to establish and implement long-term interventions to help reduce anxiety and depression among kidney transplant recipients.

The limitations of this study include the inclusion of only studies published in English and the inability to confirm the effect size of medication adherence due to differences in measurement methods among the selected studies. Therefore, caution is needed when interpreting the results. Additionally, due to the small number of included studies, a fixed-effects model was used for the meta-analysis; however, the results generally indicated high heterogeneity. Future studies should apply stricter controls in nurse-led intervention methods and procedures. Despite these limitations, this study is significant in that it analyzed only RCT studies confirming the effectiveness of nurse-led interventions for kidney transplant recipients and identified the detailed contents of various nurse-led interventions, which can serve as foundational evidence for future intervention development.

Conclusion

This study analyzed the effects of nurse-led interventions on quality of life, medication adherence, anxiety, and depression in kidney transplant recipients, based on eight RCTs involving a total of 477 participants, published up until October 2023. The aim was to provide objective evidence for the usefulness of nurse-led interventions. The study results indicated that the quality of life measured within 1~2 months improved in the group that received nurse-led interventions. Additionally, nurse-led interventions were found to enhance medication adherence among kidney transplant recipients, suggesting the necessity for early intervention by

nurses. Anxiety, and depression levels were shown to have decreased over time, indicating that prolonged intervention is more effective in enhancing psychological stability in kidney transplant recipients. Therefore, nursing interventions for kidney transplant recipients should be long-term, combining education for information provision and counseling to alleviate psychological conditions.

Through this study, the importance of the nurse's role in ensuring successful kidney transplants was recognized, highlighting the need to establish strategies for providing continuous nursing interventions. However, since all the studies included in this meta-analysis were conducted overseas, future research should reflect domestic circumstances by developing and applying nurse-led interventions using the RCT methodology to verify their effectiveness.

Author contributions

SY Park: Conceptualization, Methodology, Data curation, Analysis, Supervision, Visualization, Writing - original draft, Writing - review & editing. LH Kwak: Conceptualization, Methodology, Data curation, Analysis, Investigation, Visualization, Writing - original draft, Writing - review & editing.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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Supplementary materials

Appendix 1

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Appendix 1. List of Studies included in Meta-Analysis

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