
Article

Effects of Integrated Indirect Forest Therapy on Emotion, Fatigue, Stress, and Immune Function in Hemodialysis Patients

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Abstract: (1) Background: Most hemodialysis patients may experience physiological and psychological stress. Exposure to nature has been previously reported to reduce the measures of psychological and physiological stress, and immune function. This study aimed to investigate psychological and physiological effects of integrated indirect forest therapy on chronic renal failure patients undergoing hemodialysis. (2) Methods: As a quasi-experiment, this study employed a nonequivalent control group, repeated measurements, and a non-synchronized design. A total of 54 participants were included: 26 and 28 in the experimental and control groups, respectively. During hemodialysis, five types of forest therapy stimuli (visual, auditory, olfactory, tactile, and motor) were applied 3 times per week for 4 weeks during 15-minute sessions. (3) Results: Positive but not negative emotion measures differed between the groups after the intervention. Fatigue and physiological stress levels were significantly reduced in the experimental group, whereas no significant difference was found between the groups on the measures of psychological stress. Activation of both the parasympathetic and sympathetic nervous systems was similar in both groups, as was the number of natural killer cells. (4) Conclusion: Integrated indirect forest therapy may help increase positive emotions and reduce fatigue and stress levels during hemodialysis in patients with chronic renal failure.

Keywords: hemodialysis; indirect forest therapy; emotion; fatigue; stress; heart rate variability; natural killer cells

1. Introduction

Chronic renal failure is an irreversible disease associated with gradual loss of kidney function [1]. In Korea, affected patients tend to choose hemodialysis (81,760 [75.1%] patients), rather than renal transplant or peritoneal dialysis [2]. Without a transplant, most hemodialysis patients continue to undergo dialysis over 4–5 hours for 3–4 times per week for the rest of their life [3].

During hemodialysis, patients may experience physiological and psychological stress due to restrictions that prevent them from maintaining their daily routines [4]. The primary factor that causes the patients' stress is fatigue [5]. Seventy-nine percent of hemodialysis participants complain of fatigue [6], which tends to increase after hemodialysis [7]. Concurrently, psychological stress in hemodialysis patients tends to be caused by tensions provoked by dependence on hemodialysis machines [8], loss of pride, uncertainty about the future, and feelings of guilt toward family [9], among others. Indeed, previous studies have shown that stress levels in hemodialysis patients are as high as those in patients with terminal cancer [10]. Severe and prolonged stress response may lead to the suppression of the immune system function [11]. Therefore, it is critical to develop stress management interventions for hemodialysis patients.

Stress reduction theory has been proposed by Ulrich; it aims to explain how the natural environment reduces the human response to mental and physical stress, for example, during the sequential process of viewing nature scenes, which may influence one's emotions and behavior [12]. According to this theory, an individual exposed to visual stimuli associated with the natural environment is likely to experience immediate and general emotional and automatic behavioral response [12]. For example, if the observer is stressed, a view of nature can attract attention and block or reduce stressful thoughts, thus promoting psychophysiological recovery [13]. In line with this

theory, forest therapy has been attracting attention; some studies suggest that it promotes physical health and may strengthen the immune system [14], while others show that it may improve mental and physical health [15], affecting physiological and psychological parameters. Managed by the autonomic nervous system, heart rate variability (HRV) is a biomarker of stress [16]. Previous studies have indicated that forest therapy may activate the parasympathetic and inhibit the sympathetic nervous system responses [17,18]; moreover, it has also been shown to affect immune function [19], specifically, to increase the activity of natural killer cells (NK) [20].

Indirect forest therapy involves providing patients indoors with forest-like stimuli [21]. Psychological and physiological stress levels have been shown to alleviate in response to just viewing nature scenes [22, 23]; however, patients tend to prefer receiving both visual and auditory stimuli at the same time (e.g., seeing a nature view while listening to water sounds) [24]. Moreover, olfactory stimulation with wood-scented oil significantly increased parasympathetic activity [25]. Although few studies exist on tactile stimulation, touching wood with feet has been shown to have a positive impact on brain activity and to promote physiological relaxation [26]. In a study that applied an electric leg exercise machine to patients undergoing hemodialysis in a supine position, the patients' mental health index score increased significantly, which suggests that this could be a safe and effective intervention [27].

Recent studies of indirect forest therapy mostly focused on healthy individuals [15,18,21]; few such studies have been performed in a clinical context [28, 29]. Studies of indirect forest therapy that involve five senses are rare, despite evidence that this approach is more effective than that involving only one or two senses [30]. In fact, in a study of older adults, Park [31] reported that stimulating five stimuli might be more effective than stimulating only one or two of the senses in indirect forest therapy [30].

Hemodialysis patients have restricted access to nature due to their treatment and deconditioning schedule. Exposing patients to nature-associated sensory stimuli while they remain in a hospital environment may help bring to them the physiological and psychological benefits of forest therapy. This study aimed to verify the effects of integrated indirect forest therapy on the measures of emotion, fatigue, and stress; HRV; and NK cell count in patients with chronic renal failure undergoing hemodialysis.

2. Materials and Methods

2.1. Participants

In this quasi-experimental study with a nonequivalent control group, repeated measurements, and a non-synchronized design, 130 patients with chronic renal failure and undergoing hemodialysis at a designated unit of a medical clinic were selected using convenience sampling.

Using repeated measures ANOVA with G*Power 3.1 software [32], we determined that 56 individuals in total (28 per group) were required for the present study, given a significance level of .05, effect size of .15 [33], and statistical power of .80. Accounting for possible dropouts, we included a total of 64 (32 per group) participants. In the experimental group, 2 participants changed clinics, 1 withdrew, and 3 failed to meet the compliance rate of the experimental group, resulting in the final group size of 26. In the control group, 1 participant changed clinics, 1 experienced health deterioration, and 2 missed hemodialysis sessions, resulting in the final group size of 28. Overall, 54 participants were included in the study, and the dropout rate was 15.6%.

2.2. Materials

Demographic and clinical characteristics of interest included age, sex, marital status, education level, occupation, religion, cause of disease, period of hemodialysis, vascular state for hemodialysis, and hemodialysis vessel location.

Emotion. The inventory of personal reactions developed by Zuckerman (ZIPERS) [34] was used to examine emotional reactions toward indirect forest environments. Among 12 items of ZIPERS, items #1 to #6 represented *positive emotions* and items #7 to #12 represented *negative emotions* [35]. The total score ranged from 0 to 30 points, with higher scores indicating that the individual has more

positive and negative emotions. In our study, Cronbach's alpha was .62 and .90 for the positive and negative emotion components, respectively, with previously reported values ranging from .80 to .85 [34].

Fatigue. Fatigue was measured using a tool proposed by Lee et al. [36] and revised and updated by Kim [37]. Of 17 items, a single item was eliminated as it was not suitable for the present study [38]. The total score ranged from 0 (not fatigued at all) to 160 (extremely fatigued) points, measured on a 10-point Likert scale. In our study, Cronbach's alpha was .83, while the previously reported values ranging from .94 to .96 [36].

Stress. Stress levels were measured using a tool developed for hemodialysis patients by Kim [39] and revised and updated by Choi [40]. The tool includes 20 items in total, with physiological and psychological stress interrogated by a set of 10 questions each. Using 4-point Likert scales, the stress scores yielded by this tool ranged from 10 (not serious at all) to 40 (extremely serious) points. In our study, Cronbach's alpha was .86 for both physiological and psychological stress levels. In Choi's study, Cronbach's alpha for physiological stress and psychological stress was .86 and .79, respectively [40].

To assess the physiological indicator of stress, we used minimum changes in heart rate, measured using an HRV meter (Wise-8000T); autonomic nerve responses were observed. HRV measured parameters such as sympathetic nervous system activity (low frequency) and parasympathetic nervous activity (high frequency). The normal range of the sympathetic and parasympathetic nervous system activity is within low (0.04–0.15 Hz) and high (0.15–0.4 Hz) frequency values, with the corresponding power spectrum of 5.9–8.0 and 3.8–7.0, respectively.

NK cell. The immune function was measured using flow cytometry to assess the NK cell (CD16+CD56) levels. To this end, 3 mL of blood was collected in ethylenediaminetetraacetic acid (EDTA) tubes and sent to the S laboratory.

2.3. Indirect Forest Therapy

We used visual, auditory, olfactory, tactile, and motor stimulation with all participants (Figure 1). For visual and auditory stimulation, a TV screen was used to play images and sounds of nature, while olfactory stimulation was concurrently provided by placing a cotton pad with drops of cypress oil on the right shoulder of each participant. For tactile stimulation, we simulated walking on wood using an electric leg exercise machine set up with paulownia wood.

These sessions were delivered during hemodialysis. A total of 13 sessions were performed, including three 15-minute sessions per week over 4 weeks, as determined by the hemodialysis schedule. The program was started 3 hours after hemodialysis began, as patients were expected to have the highest levels of stress, fatigue, and other physiological changes between 3–4 hours after hemodialysis start [41]. The program was performed under the supervision of healthcare staff.

2.4. Data Collection

This study was approved by the Human Clinical Research Ethics Committee of K University (Approval No.: KWNUIRB-2019-12-003-001). Informed consent was obtained from the participants and the study adhered to the Declaration of Helsinki.

Data collection took place between January 13 and March 31, 2020. Levels of emotion, fatigue, stress, and HRV of the patients in the control group were evaluated at baseline and during weeks 2 and 4. Levels of emotion, fatigue, and stress were measured by self-report. When measuring HRV, the participants were instructed to remain still. Subsequently, the program was delivered to the experimental group, where the same schedule was followed. Levels of NK cells were measured at baseline and in week 4 in both groups.



Figure 1. Patients participating in integrated indirect forest therapy program while undergoing hemodialysis

2.5. Statistical Analysis

Data analysis was performed using SPSS software 24.0 (IBM Corporation, Armonk, NY, USA). Homogeneity between experimental and control groups was examined using the independent t-test, χ^2 test, and Fisher's exact test. To determine program effects, a dependent variable that met the normality of distribution assumption (measure of fatigue) was tested using the repeated measures ANOVA. Other dependent variables that did not meet the normality of distribution assumption (measures of positive emotions, negative emotions, physiological stress, psychological stress, parasympathetic nervous activity, and sympathetic nervous activity) were analyzed using the generalized estimate equation. Finally, between-group differences in program effects on NK cell levels were analyzed using the independent t-test.

3. Results

There was no significant between-group difference in demographic characteristics (Table 1). Furthermore, the results of homogeneity tests for participants' positive and negative emotions, fatigue, physiological and psychological stress, activation of sympathetic and parasympathetic nervous systems, and NK cell levels showed no significant difference between the groups at baseline (Table 2).

Table 1. Demographic and clinical characteristics of the groups (N=54)

Characteristics	Categories	Exp.(n=26)	Cont.(n=28)	χ^2 or z	p
		Mean \pm SD/n(%)	Mean \pm SD/n(%)		
Age (year)		60.35 \pm 2.37	56.89 \pm 2.68	27.63	.640
Gender	Male	18(69.2)	22(78.6)	0.61	.434
	Female	8(30.8)	6(21.4)		
Marital status	Married	23(88.5)	22(78.6)	0.95	.470 [†]
	Single	3(11.5)	6(21.4)		
Education	<Middle	8(30.8)	6(21.4)	0.79	.675
	High	7(26.9)	10(35.7)		
	University	11(42.3)	12(42.9)		
Occupation	Yes	12(46.2)	11(39.3)	0.26	.610
	No	14(53.8)	18(60.7)		
Religion	Yes	16(61.5)	18(64.3)	0.04	.835
	No	10(38.5)	10(35.7)		
Cause of disease	Diabetes	12(46.2)	10(35.7)	1.25	.535
	Hypertension	9(34.6)	9(32.1)		
	etc.	5(19.2)	9(32.1)		
Period of hemodialysis (year)	< 5	16(61.5)	14(50.0)	0.73	.394
	\geq 5	10(38.5)	14(50.0)		
Vascular state for hemodialysis	Fistula	23(88.5)	25(89.3)	0.01	>.999 [†]
	Graft	3(11.5)	3(10.7)		
Hemodialysis vessel location	Upper arm	9(34.6)	7(25.0)	0.60	.439
	Forearm	17(65.4)	21(75.0)		

Cont.=control group; Exp.=experimental group; SD=standard deviation; [†]Fisher's exact test

Table 2. Values of dependent variables for the groups (N=54)

Variables		Exp.(n=26)	Cont.(n=28)	t	p
		Mean \pm SD	Mean \pm SD		
Emotion	Positive emotion	19.46 \pm 6.24	18.82 \pm 6.15	-0.38	.706
	Negative emotion	4.89 \pm 7.80	4.36 \pm 4.79		
Fatigue		63.62 \pm 28.14	62.39 \pm 27.58	-0.16	.873
Stress	Physiological stress	18.19 \pm 5.84	18.57 \pm 5.74	0.24	.811
	Psychological stress	21.85 \pm 7.42	21.14 \pm 5.90		
HRV	High frequency(HF)	6.48 \pm 0.71	6.45 \pm 0.96	-0.15	.883
	Low frequency(LF)	6.76 \pm 0.34	6.72 \pm 0.54		
NK cells(%)	CD16+CD56	11.80 \pm 6.64	14.24 \pm 9.82	1.06	.295

Cont.=control group; Exp.=experimental group; HRV=heart rate variability; NK cell= natural killer cell; SD=standard deviation

3.2. Effects of Indirect Forest Therapy

For measures of positive emotion, the interaction between group and measurement time was significantly different ($\chi^2=7.26$, $p=.027$) (Figure 2, a), whereas, for measures of negative emotion, there was no significant difference in this interaction ($\chi^2=3.63$, $p=.163$) (Table 3). Similarly, for measures of fatigue, there was a significant interaction between group and measurement time ($F=3.75$, $p=.027$) (Figure 2, b). There was a significant difference in interaction between group and measurement time for the measures of physiological stress ($\chi^2=9.60$, $p=.008$) (Figure 2, c), whereas no such difference in interaction was observed for the measures of psychological stress ($\chi^2=0.84$, $p=.657$). There was also no significant difference in interaction between group and measurement time for the activation of either parasympathetic ($\chi^2=4.92$, $p=.085$) or sympathetic ($\chi^2=3.34$, $p=.189$) nervous system (Table 3). The difference in the number of NK cells between the groups was not statistically significant ($t=0.45$, $p=.655$) (Table 4).

Table 3. Effect of indirect forest therapy on emotion, fatigue, stress and HRV (N=54)

Variables			Exp.(n=26)	Cont.(n=28)	source	F or χ^2	p
			Mean±SD	Mean±SD			
Emotion	Positive emotion	T0	19.46±6.24	18.82±6.15	Group	5.74	.017
		T1	21.73±6.02	17.93±6.06	Time	0.87	.648
		T2	22.12±5.19	16.86±5.84	Group*Time	7.26	.027 [†]
	Negative emotion	T0	4.89±7.80	4.36±4.79	Group	2.12	.145
		T1	3.73±6.42	4.61±5.38	Time	0.22	.898
		T2	3.54±5.44	5.68±6.42	Group*Time	3.63	.163 [†]
Fatigue	T0	63.62±28.14	62.39±27.58	Group	1.35	.251	
	T1	59.81±22.07	67.61±27.80	Time	0.24	.788	
	T2	57.15±25.63	73.11±31.04	Group*Time	3.75	.027	
Stress	Physiological stress	T0	18.19±5.84	18.57±5.74	Group	1.87	.171
		T1	16.77±5.54	18.54±5.20	Time	2.97	.227
		T2	16.50±5.18	20.11±6.46	Group*Time	9.60	.008 [†]
	Psychological stress	T0	21.85±7.42	21.14±5.90	Group	0.30	.584
		T1	21.58±5.99	21.11±6.29	Time	0.35	.838
		T2	21.85±6.65	20.39±6.81	Group*Time	0.84	.657 [†]
HRV	High frequency	T0	6.48±0.71	6.45±0.96	Group	1.26	.261
		T1	6.94±1.09	6.41±0.90	Time	5.12	.077
		T2	6.55±0.95	6.36±0.94	Group*Time	4.92	.085 [†]
	Low frequency	T0	6.76±0.34	6.72±0.54	Group	0.81	.368
		T1	6.94±0.49	6.73±0.51	Time	3.30	.192
		T2	6.79±0.46	6.73±0.53	Group*Time	3.34	.189 [†]

Cont.=control group; Exp.=experimental group; HRV=heart rate variability; NK cell=natural killer cell; SD=standard deviation; T0=baseline assessment; T1=2nd week of the program; T2=4th week of the program[†] generalized estimate equation

Table 4. Effect of indirect forest therapy on NK cell levels (N=54)

Variables	Group	Pretest	Posttest	Mean difference	t	p
		Mean±SD	Mean±SD	Mean±SD		
NK cell(%)	Exp.(n=26)	11.80±6.64	11.18±5.94	-0.62±2.09	0.45	.655
	Cont.(n=28)	14.24±9.82	13.21±8.82	-1.02±4.09		

Cont.=control group; Exp.=experimental group; NK cells= natural killer cells; SD=standard deviation.

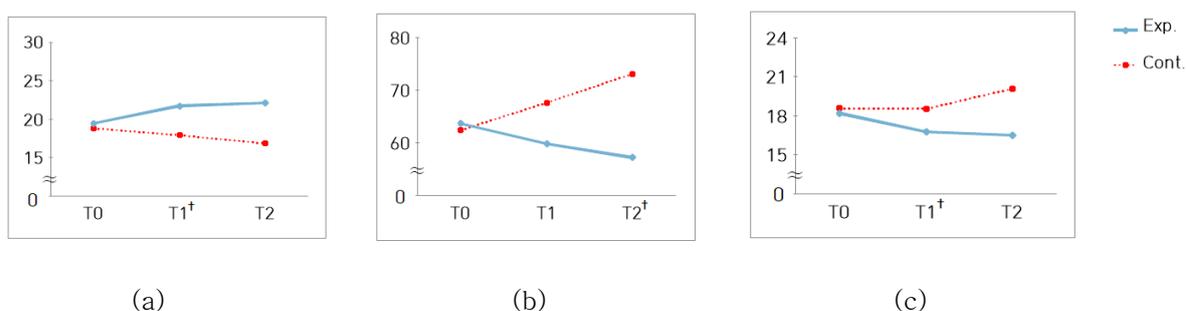


Figure 2. Changes to the measures of positive emotion (a), fatigue (b), physiological stress (c) in both groups T0=baseline assessment; T1=2nd week of the program; T2=4th week of the program; † $p < 0.05$

4. Discussion

This study aimed to identify the psychological and physiological effects of an integrated indirect forest therapy program on hemodialysis patients' measures of emotion, fatigue, stress, and immune function. In the present study, indirect forest therapy simultaneously stimulated five senses of patients undergoing hemodialysis, providing a simulation of the outdoors to individuals needing to remain in a hospital.

In our study, the measures of positive emotions increased after integrated indirect forest therapy, thus these changes were statistically significant. Previously, Hwang and Park [42] presented a slideshow of nature-related images to college students and found significant changes in their emotional states. Yi [43] compared urban views and nature views to establish which group of images may perform better at triggering positive emotions. In addition, Lee [35] suggested that individuals would be positively impacted if they felt the environment would give them *positive effects*. To summarize, integrated indirect forest therapy could be applied to patients who experience emotional distress due to hemodialysis to increase their positive emotions.

The impact of indirect forest therapy on decreasing levels of fatigue has been previously reported in several studies [37, 44, 45]. Park [46] found psychological changes in college students exposed to the views of forests, and Jeon [21] reported that indirect forest therapy may reduce the levels of tiredness. In our study, fatigue was significantly reduced in the experimental group compared to that of the control group. Hemodialysis patients are likely to experience high levels of fatigue; indirect forest therapy may be an effective fatigue management tool, provided it is continuously applied in a clinical setting.

In this study, physiological stress levels were significantly reduced compared those of the control group. However, psychological stress measures were marginally influenced by indirect forest therapy. Hwang and Park's [42] study of indirect forest visual stimulation in college students as well as that by Yi et al. [43] reported significant results. In both studies, stress was significantly reduced by indirect forest therapy. Since the participants of our study were patients with chronic renal failure, it is expected that there will be differences in psychological stress among university students. In particular, in the present study, the levels of psychological stress were higher than those of physiological stress; this finding is consistent with that of Kim and Yang's [4] studies, whereby hemodialysis patients had high levels of psychosocial stress.

In the present study there was no significant difference in either parasympathetic or sympathetic activity between before and after the intervention, as measured by HRV. Previously, Alvarsson et al.

[47] reported that parasympathetic activity was not influenced by auditory stimulation with forest-associated sounds. However, Igarashi et al. [48] and Ikei et al. [49] have shown that parasympathetic activity was affected by olfactory and tactile stimulation, respectively, resulting in physiological relaxation. A study by Jo et al. [50] has shown a significant decrease in stress levels as a result of decreased activation of the sympathetic nervous system. Given the discrepancies in previous study findings, further research is required to determine the impact of indirect forest therapy types on nervous system activity.

Playing a key part in the immune system, NK cells are sensitive to stress [19]; higher levels of stress may reduce the activity of NK cells [51]. In our study, integrated indirect forest therapy did not affect NK cell levels. This result was different from that of a previous study, which reported higher levels of NK cell activation in a forest meditation group than the control group [20]. In addition, a 12-week high-intensity forest walking intervention has been previously reported to significantly increase the number of NK cells [52]. A study that applied a three-day bamboo forest therapy in male students also reported that their NK cell levels increased following this intervention [53]. Since our study applied indirect forest therapy for 4 weeks, its effects are likely to be different from those previously reported. Given that NK cell activation of hemodialysis patients tends to be lower than that of healthy individuals [54], it is advisable to apply the present program over a longer period of time and to re-examine its effect on immunity.

Participants in the experimental group reported that the program helped them feel like the hemodialysis session went faster than usual, and they were satisfied with the experience of “being in nature.” This finding suggests that indirect forest therapy may be useful to patients undergoing hemodialysis and those undergoing other forms of long-term treatment, for example, chemotherapy.

This study has several limitations. First, it was difficult to control the impact of other environmental conditions, including the sounds of hemodialysis machines and other medical equipment, which may have affected the presented findings. Second, the participants were not randomly assigned to the experimental and control groups. Randomized controlled trials should be conducted in the future. Third, hemodialysis patients find it difficult to remain still while undergoing hemodialysis, resulting in movements that may have influenced the HRV values. Fourth, immune function was measured with a single index, specifically, NK cell levels. Future studies should use other indicators to examine the impact of indirect forest therapy on the immune function.

5. Conclusions

Indirect forest therapy may promote positive emotions and reduce the levels of fatigue and stress in patients undergoing hemodialysis. This intervention may also help patients relax and rest during their treatment.

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