The Role of Group Supportive Psychotherapy on Quality of Life and Its Relationship with Heart Rate Variability and Blood Serotonin Levels in End-Stage Renal Disease (ESRD) Patients Undergoing Chronic Hemodialysis

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ABSTRACT

***Background*:** *Patients with end-stage renal disease (ESRD) undergoing chronic hemodialysis often experience reduced quality of life and autonomic dysregulation. Group supportive psychotherapy may improve psychological well-being through biopsychosocial mechanisms. This study evaluated the effects of group supportive psychotherapy on quality of life and its association with heart rate variability (HRV) and blood serotonin levels.* **Methods:** *This randomized, parallel-group, single-blind controlled trial was conducted at the Hemodialysis Unit of Dr. Cipto Mangunkusumo National General Hospital, Jakarta, from November 2024 to January 2025. Fifty-two eligible patients were randomly assigned to an intervention group receiving group supportive psychotherapy plus standard care (n = 26) or a control group receiving standard care alone (n = 26). Outcomes were assessed at baseline and post-intervention using Kidney Disease Quality of Life-36 (KDQOL-36), HRV measured by standard deviation of normal-to-normal intervals (SDNN), and plasma serotonin levels measured using enzyme-linked immunosorbent assay (ELISA). Statistical analyses included an independent t-test or Mann-Whitney test, with effect size calculation and ANCOVA adjustment for baseline values.* **Results:** *The intervention group demonstrated significantly greater improvement in KDQOL-36 scores compared with control (mean change 8.46-16.92 vs 0.27-11.36; p=0.046). After adjustment, the between-group*

difference remained statistically significant (p<0.001), with a large effect size (Cohen's d = 1.16). Plasma serotonin levels were significantly higher in the intervention at post-intervention (p=0.028; r=0.30). However, no significant differences were observed in HRV (SDNN) either between groups (p=0.805) or within groups over time (p>0.05). **Conclusion:** *Group supportive psychotherapy significantly improves quality of life and is associated with higher plasma serotonin levels in ESRD patients undergoing chronic hemodialysis. However, no significant autonomic modulation, as measured by HRV, was demonstrated.*

Keywords: *End-stage renal disease, group supportive psychotherapy, hemodialysis, heart rate variability, quality of life, serotonin.*

INTRODUCTION

End-stage renal disease (ESRD) represents the terminal stage of chronic kidney disease and requires renal replacement therapy for survival.[1,2] Despite advances in hemodialysis, patients continue to experience substantial physical symptom burden, psychological distress, and diminished quality of life (QoL). Depression and anxiety affect individuals undergoing dialysis, contributing to poor treatment adherence and increased morbidity. [3]

Beyond psychosocial impairment, ESRD has been associated with autonomic nervous system dysfunction and neurobiological alterations. [4] Reduced heart rate variability (HRV), particularly SDNN, reflects impaired autonomic regulation and has been linked to adverse cardiovascular outcomes.[3] Additionally, serotonin dysregulation may contribute to mood disturbances and systemic inflammatory processes. [5]

Supportive psychotherapy is a structured, patient-centered intervention aimed at strengthening coping mechanisms, emotional regulation, and adaptive functioning. When delivered in group format, it also provides peer validation and social reinforcement. Emerging evidence suggests that psychotherapeutic interventions may influence psychophysiological processes, potentially through psycho-neuro-immuno-endocrinology (PNIE) pathways. [6,7]

However, experimental evidence linking psychotherapy to both psychological and physiological biomarkers in ESRD remains limited.[6,7] This study, therefore, aimed to evaluate the effect of group supportive psychotherapy on quality of life, HRV, and plasma serotonin levels in patients undergoing chronic hemodialysis.

METHODS

Study Design and Setting

This study was a single-center, single-blind, parallel-group randomized controlled trial (RCT) with a 1:1 allocation ratio comparing group supportive psychotherapy plus standard hemodialysis care versus standard hemodialysis care alone. The study was conducted at the Hemodialysis Unit, Dr. Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, from November 2024 to January 2025.

Ethical approval was obtained from the Ethics Committee of the Faculty of Medicine, Universitas Indonesia, Dr. Cipto Mangunkusumo National General Hospital (Approval No. KET-1455/UN2.F1/ETIK/PPM. 00.02/2024).

Written informed consent was obtained from all participants.

Study Population

The inclusion criteria encompass patients diagnosed with end-stage renal disease (ESRD) receiving chronic hemodialysis biweekly in the non-Hepatitis section of the Hemodialysis Unit, Dr. Cipto Mangunkusumo, Central Jakarta, from November 2024 to January 2025. Patients must possess the ability to communicate, demonstrate a willingness to complete questionnaires, engage in group supportive psychotherapy, and sign both the informed consent and an additional agreement to participate in the study. The exclusion criteria encompass patients with psychosis, acute medical illnesses, cognitive impairment, hearing impairment, hepatitis B patients receiving chronic hemodialysis at a designated hemodialysis facility for hepatitis patients, and individuals who do not have Bahasa Indonesia as their primary language.

Study Procedures

Participants who met the inclusion criteria and agreed to participate were enrolled after providing written informed consent. Baseline data collection was conducted before hemodialysis and included demographic and clinical characteristics, heart rate variability (HRV) measurement, plasma serotonin assessment, and completion of the Kidney Disease Quality of Life-36 (KDQOL-36) questionnaire.

Participants assigned to the intervention group received group supportive psychotherapy in addition to routine pharmacological treatment and scheduled chronic hemodialysis. Participants in this group were divided into psychotherapy groups consisting of 8–9 participants based on their hemodialysis schedules. Psychotherapy sessions were conducted once weekly for five consecutive weeks, with each session lasting approximately 45–60 minutes. Sessions were delivered after completion of hemodialysis in a designated discussion room within the hemodialysis unit, with participants seated in a circular arrangement to facilitate structured group interaction. The psychotherapy sessions were delivered by a trained and certified psychotherapist from the Psychosomatic and Palliative Division who had completed formal training in psychodynamic psychotherapy and additional training in supportive group psychotherapy.

Participants in the control group received routine pharmacological therapy and standard chronic hemodialysis care without additional psychotherapy intervention. After completion of the intervention period, outcome assessments were repeated using the same standardized procedures applied at baseline.

Outcome Measure

The primary outcome of this study was quality of life. Quality of life was defined as an individual's perception of their position in life within the context of the cultural and value systems in which they live and in relation to their goals, expectations, standards, and concerns. In this study, quality of life among patients with end-stage renal disease undergoing chronic hemodialysis was assessed using the KDQOL-36 questionnaire.

The secondary outcome included HRV and plasma serotonin levels. HRV was defined as the variation in time intervals between consecutive heartbeats and was assessed using time-domain analysis, specifically the SDNN obtained from a 5-minute HRV recording before hemodialysis.

Blood samples for serotonin measurement were collected before hemodialysis sessions. Whenever feasible, sampling was performed in the morning to reduce circadian variability. However, strict control of fasting status and circadian timing was not consistently applied. Blood samples were processed using standard laboratory protocols, centrifuged to obtain plasma, and stored under controlled conditions prior to analysis using enzyme-linked immunosorbent assay (ELISA).

All outcome measurements were performed at baseline (pre-intervention) and after completion of the five-session intervention (post-intervention).

Sample Process

Participants were recruited using consecutive sampling among patients undergoing chronic hemodialysis who met the eligibility criteria. Randomization was performed using computerized block randomization generated by an independent statistical analyst to ensure balanced allocation between groups. Allocation was implemented using a sequential numbering system based on participant order numbers. Allocation concealment was ensured using sequentially numbered opaque envelopes prepared by the independent statistician.

To minimize contamination bias, randomization considered hemodialysis schedules so that participants in the intervention and control groups attended different dialysis sessions. This strategy prevented interaction or discussion between participants from different groups during the intervention period.

This study employed a single-blind design. The investigator responsible for participant enrollment and baseline data collection was blinded to group allocation during the assignment process. In addition, participants from different groups attended separate hemodialysis sessions and were not informed about the intervention schedule or procedures received by the other

group, thereby reducing the risk of performance and contamination bias. Due to the behavioral nature of the psychotherapy intervention, the treating psychotherapist was not blinded. Outcome assessment, including KDQOL-36 scoring, HRV measurement, and laboratory analysis of plasma serotonin levels, was performed by personnel who were not involved in the intervention delivery and were blinded to group allocation.

Participants were subsequently assigned to either the intervention group or the control group according to the randomization sequence. Participants allocated to the intervention group were further divided into psychotherapy groups consisting of 8–9 participants based on their hemodialysis schedules.

Statistical Analysis

Statistical analysis was performed using SPSS version 25.0. Baseline characteristics of the study participants were summarized in tabular form. Categorical variables were presented as frequencies and percentages, while numerical variables were expressed as medians with interquartile ranges or means with standard deviations, as appropriate.

The normality of data distribution was assessed using the Shapiro-Wilk test due to the relatively small sample size in each group (≤50 participants). For comparisons between groups, independent t-tests were used for normally distributed numerical variables, whereas the Mann-Whitney U test was applied for non-normally distributed variables.

Within-group comparisons between pre- and post-intervention measurements were analyzed using paired t-tests for normally distributed variables or Wilcoxon signed-rank tests for non-normally distributed variables. All statistical tests were two-tailed, and a p-value <0.05 was considered statistically significant.

RESULTS

Participant Flow

A total of 56 patients with end-stage renal disease undergoing chronic hemodialysis were assessed for eligibility. After screening and randomization, 52 participants completed the study and were included in the final analysis, with 26 participants allocated to the intervention group and 26 participants to the control group. The participant recruitment and allocation process is illustrated in **Figure 1.**

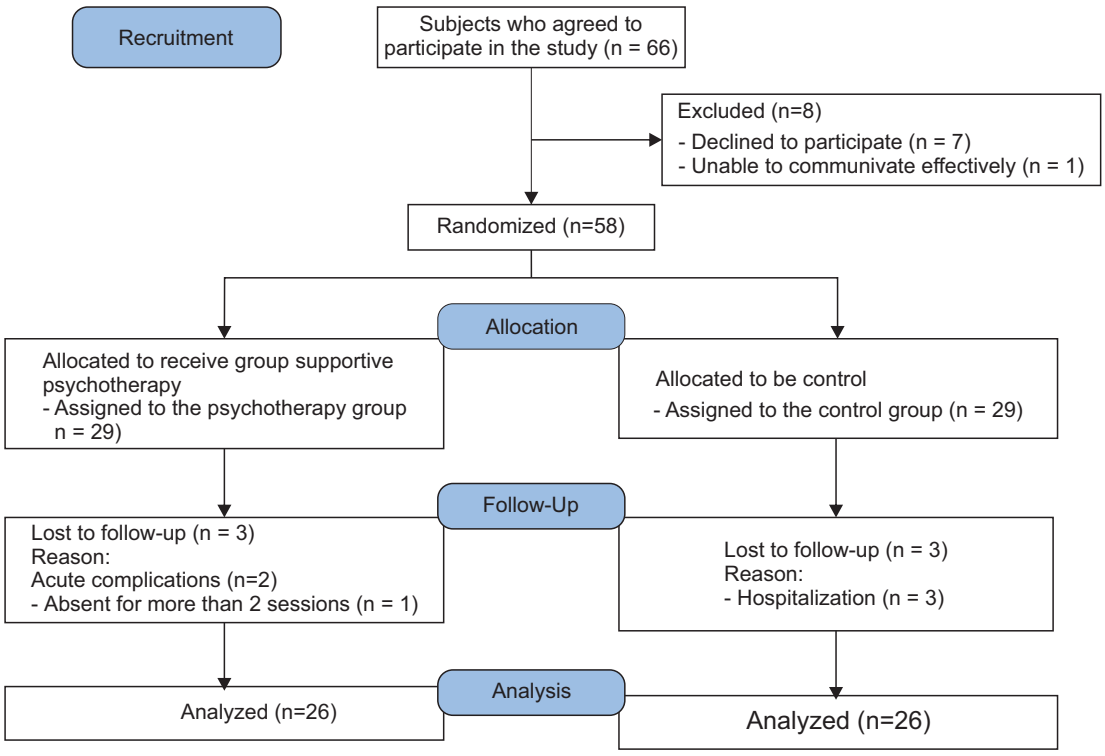

Figure 1. Subject Recruitment Flowchart

Baseline Characteristics

Baseline demographic and clinical characteristics of the participants are presented in **Table 1**. Overall, the characteristics of participants in the intervention and control groups were comparable.

Hypertension was the most common comorbidity in both groups, affecting 15 participants (57.7%) in the intervention group and 13 participants (50%) in the control group. Diabetes mellitus was present in 9 participants (34.6%) in the intervention group and 6 participants (23.1%) in the control group. The majority of participants in both groups were receiving five or more medications, including 23 participants (88.46%) in the intervention group and 22 participants (84.61%) in the control group.

Table 1. Baseline Characteristics of Study Subjects

Characteristics	Group Supportive Psychotherapy (n=26)	Control (n=26)
Gender, n (%)		
Male	17 (6.4)	18 (69.2)
Female	9 (34.6)	8 (30.8)
Age (year), mean (SD)	41.08 (SD 15.21)	47.38 (SD 15.40)
Education levels, n (%)		
Elementary school	1 (3.8)	0 (0.0)
Junior high school	1 (3.8)	7 (26.9)
Senior high school	14 (53.8)	10 (38.5)
University	10 (38.5)	9 (34.6)
Duration of ESRD, median (IQR)	6 (3.75 – 15.5)	5 (3 – 9)
Duration of ESRD, n (%)		
< 5 years	7 (26.9)	9 (34.6)
≥ 5 years	19 (73.1)	17 (65.4)
Hemodialysis frequency, median (IQR)	5 (3.12 – 7.0)	4 (2 – 6.25)
Duration of hemodialysis, n (%)		
< 1 year	0 (0.0)	0 (0.0)
≥ 1 year	26 (100.0)	26 (100.0)
Hemodialysis cycle, median (IQR)	2 (2 – 2)	2 (2 – 2)
Hemodialysis cycle, n (%)		
≤ 2x per week	26 (100.0)	26 (100.0)
> 2x per week	0 (0.0)	0 (0.0)
Hemodialysis duration, median (IQR)	5 (5 – 5)	5 (5 – 5)
Hemodialysis duration, n (%)		
< 4 hours	0 (0.0)	0 (0.0)
≥ 4 hours	26 (100.0)	26 (100.0)
Hemodialysis access changes, n (%)		
Yes	17 (65.4)	15 (57.7)
No	9 (34.6)	11 (42.3)
Comorbidities, n (%)		
Diabetes mellitus	9 (34.6)	6 (23.1)
Hypertension	15 (57.7)	13 (50.0)
SNNT	1 (3.8)	1 (3.8)
Autoimmune disease	1 (3.8)	1 (3.8)
Nefrolithiasis	1 (3.8)	3 (11.4)
Others	1 (3.8)	0 (0.0)
Number of comorbidities, n (%)		
< 3	25 (96.2)	26 (100.0)
≥ 3	1 (3.8)	0 (0.0)
Number of medications, n (%)		
< 5 jenis	2 (7.69%)	4 (15.38%)
≥ 5 jenis	23 (88.46%)	22 (84.61%)
KDQOL-36 scores pre, mean (SD)	60.17 (SD 10.65)	56.22 (SD 8.84)
HRV pre, Median (IQR)	22.86 (15.29 – 32.99)	24.88 (13.24 – 39.30)
High	5 (19.2)	7 (26.9)
Low	11 (42.3)	9 (34.6)
Very low	10 (38.5)	10 (38.5)
Serotonin Plasma Levels pre, Median (IQR)	221.65 (148.98 – 320.65)	211.10 (172.52 – 322.72)

Effect of Group Supportive Psychotherapy on Quality of Life

The effect of group supportive psychotherapy on quality of life measured using KDQOL-36 is presented in **Table 2**. At baseline, KDQOL-36 scores were comparable between groups. Following the intervention, the mean KDQOL-36 score increased to 68.64 (SD 9.59) in the intervention group, whereas the control group showed minimal change with a post-intervention score of 56.49 (SD 11.16). The difference between groups was statistically significant ($p < 0.0001$).

Within-group analysis showed a significant improvement in KDQOL-36 scores in the intervention group, whereas no significant change was observed in the control group.

Effect of Group Supportive Psychotherapy on Heart Rate Variability

The effect of group supportive psychotherapy on heart rate variability (HRV), assessed using the SDNN parameter, is presented in **Table 3**.

The median SDNN value increased in the intervention group from 22.86 (IQR 15.29–32.99) at baseline to 29.93 (IQR 15.08–42.13) after the intervention. In the control group, SDNN values showed minimal change from 24.88 (IQR 13.24–39.30) to 25.6 (IQR 15.80–38.18). However, the difference between groups was not statistically significant (p=0.805).

Effect of Group Supportive Psychotherapy on Plasma Serotonin Levels

The effect of group supportive psychotherapy on plasma serotonin levels is presented in **Table 4**.

At baseline, there was no significant difference in serotonin levels between groups. Following the intervention, serotonin levels increased in the intervention group, with a median value of 229.95 (IQR 192.07–340.45), while the control group showed lower post-intervention levels. A statistically significant difference between groups was observed (p=0.028).

Table 2. Effect of Supportive Psychotherapy on KDQOL-36

Variable	Group		p	Effect Size
	Intervention (n=26)	Control (n=26)		
KDQOL-36 score				
Pre, mean (SD)	60.17 (10.65)	56.22 (8.84)	0.152[a]	-
Post, mean (SD)	68.64 (9.59)	56.49 (11.16)	**<0.0001[a*]**	1.14[e]
Delta, mean (SD)	8.46 (16.92)	0.27 (11.36)	**0.046[a*]**	**-**

Note: a: Independent Sample T-test; *: p<0.05; e: Cohen's d

Table 3. Effect of Supportive Psychotherapy on HRV

Variable	Group		p	Effect Size
	Intervention (n=26)	Control (n=26)		
HRV				
Pre, median (IQR)	22.86 (15.29 – 32.99)	24.88 (13.24 – 39.30)	0.942[b]	-
Post, median (IQR)	29.93 (15.08 – 42.13)	25.6 (15.80 – 38.18)	0.805[b]	0.02[f]

Note: b: Mann-Whitney Test; f: r size effect

Table 4. Effect of Group Supportive Psychotherapy on Serotonin Levels

Variable	Group		p	Effect Size
	Intervention (n=26)	Control (n=26)		
Serotonin Levels				
Pre, median (IQR)	221.65 (148.98 – 320.65)	211.10 (172.52 –322.72)	0.777	-
Post, median (IQR)	229.95 (192.07 – 340.45)	197.7 (119.97–139.9)	0.028[b*]	0.30[f]

Note: b: Mann-Whitney Test; *:p < 0.05; f: r size effect

Within-Group Changes

Within-group analyses for KDQOL-36, HRV, and serotonin levels are presented in **Table 5**.

A significant improvement in KDQOL-36 scores was observed in the intervention group (p = 0.017), while no significant change was observed in the control group (p = 0.904). HRV values did not show significant changes within either group. Plasma serotonin levels showed an increasing trend in the intervention group, although the within-group change did not reach statistical significance.

DISCUSSION

Patients with ESRD undergoing chronic hemodialysis frequently experience reduced quality of life compared with the general population.[8,9] This decline is largely associated with persistent fatigue, chronic pain, psychological distress, and depressive symptoms.[9,10] Previous studies report that anxiety affects approximately 20%-30% of ESRD patients, while depression occurs in nearly 25% of this population. These findings are consistent with the baseline results of the present study, in which KDQOL-36 scores were relatively low in both groups before intervention.[11,12]

Following the intervention, patients who received group supportive psychotherapy demonstrated a significant improvement in quality of life compared with the control group. The increase in KDQOL-36 scores observed in the intervention group suggests that structured psychosocial interventions may play an important role in improving psychological well-being among patients undergoing chronic hemodialysis. The observed effect size for quality of life improvement (Cohen's d >1.0) indicates a large and clinically meaningful impact of the intervention. This suggests that the magnitude of benefit extends beyond statistical significance and may translate into noticeable improvements in patients' daily functioning and well-being. Previous studies have reported that supportive psychotherapy can positively influence coping mechanisms, treatment adherence, lifestyle behaviors, and patients' perceptions of illness burden.[13] Participation in group-based interventions allows patients to share experiences, receive emotional support from peers, and develop adaptive coping strategies, which may reduce psychological distress and improve overall well-being.[14] A systematic review and meta-analysis of psychosocial interventions in chronic illness also reported significant improvements in quality of life among participants receiving structured psychotherapy compared with usual care.[15] These findings support the potential role of supportive psychotherapy as part of a comprehensive biopsychosocial approach to ESRD management.

Heart rate variability (HRV) was evaluated using the SDNN parameter to explore potential changes in autonomic nervous system activity.[16] Although a numerical increase in SDNN values

Table 5. Effect of Group Psychotherapy on KDQOL-36, HRV, and Serotonin Levels

Variables	Group		p	Size Effect
	Pre-	Post-		
Intervention Group				
KDQOL-36 (Mean, SD)	60.17 (SD 10.65)	68.64 (SD 9.59)	0.017[c*]	0.50[e]
HRV (Median, IQR)	22.86 (15.29 – 32.99)	29.93 (15.08 – 42.13)	0.354[d]	018[f]
Serotonin (Median, IQR)	221.65 (148.98 – 320.65)	229.95 (192.07 – 340.45)	**0.058[d*]**	0.37[f]
Control Group				
KDQOL-36 (Mean, SD)	56.22 (SD 8.84)	56.49 (SD 11.16)	0.904[c]	0.02[e]
HRV (Median, IQR)	24.88 (13.24 – 39.30)	25.6 (15.80 – 38.18)	0.367[d]	0.18[f]
Serotonin (Median, IQR)	211.10 (172.52 – 322.72)	197.7 (119.97 – 39.9)	0.122[d]	0.30[f]

Note: c: Paired Sample T-test; d: Wilcoxon Test; *:p<0,05; e: Cohen's d; f: r size effect

was observed in the intervention group, the difference between groups was not statistically significant. Therefore, the present findings do not provide evidence that group supportive psychotherapy significantly improves autonomic regulation as measured by HRV in this population. The absence of a statistically significant change may be influenced by several factors known to affect HRV measurements, including age, sex, medication use, time of measurement, and lifestyle factors such as caffeine intake, smoking, physical activity, and psychological stress at the time of assessment.[17] In patients with chronic kidney disease, autonomic dysfunction is also common due to impaired baroreflex regulation, activation of the renin-angiotensin-aldosterone system, and structural cardiac changes that contribute to sympathetic overactivity and reduced parasympathetic activity.[18–21] These complex physiological mechanisms may limit the ability of short-term psychosocial interventions to produce measurable changes in HRV.

In contrast, plasma serotonin levels showed a statistically significant difference between groups following the intervention. At baseline, serotonin levels were comparable between the intervention and control groups. After completion of the psychotherapy sessions, participants in the intervention group demonstrated higher serotonin levels compared with the control group. Serotonin levels were measured in plasma samples using standardized laboratory procedures following blood collection before hemodialysis. Blood samples were obtained during routine clinical assessments to minimize procedural variability.

Serotonin plays an important role in mood regulation, stress response, and emotional processing.[5] Previous studies have suggested that psychological interventions may influence serotonergic signaling pathways associated with emotional regulation and stress adaptation. Although the present findings suggest a possible association between supportive psychotherapy and increased serotonin levels, the biological mechanisms underlying this relationship remain incompletely understood.[22–24]

Group supportive psychotherapy can function as a structured self-help group that facilitates mutual support, emotional expression, and coping reinforcement among patients with chronic illness.[25–27] Through interpersonal interaction and emotional processing, such interventions may influence psychological well-being and stress regulation. From a psycho-neuro-endocrine perspective, psychological interventions may theoretically affect neuroendocrine and immune pathways through the psycho-neuro-endocrine-immune (PNEI) network.[6,7] However, this interpretation should be considered exploratory, as inflammatory biomarkers and other immune parameters were not assessed in the present study.

This study also highlights the importance of integrating psychosocial care into the management of patients undergoing chronic hemodialysis. A multidisciplinary approach involving nephrologists, psychosomatic and palliative care specialists, psychiatrists, psychologists, and other healthcare professionals may enhance the effectiveness of supportive interventions and improve patients' overall quality of life.

Regarding methodological considerations, the study followed CONSORT recommendations for randomized clinical trials. Participant recruitment, allocation, and follow-up were documented using a CONSORT flow diagram. No significant attrition occurred after randomization.

However, several limitations should be acknowledged. First, the analysis was conducted using a per-protocol approach, which may introduce selection bias by excluding participants who did not complete the intervention, potentially overestimating the treatment effect. Second, fasting status and circadian variation were not strictly controlled during blood sampling, which may influence serotonin measurements. Furthermore, although outcome assessors were blinded, residual confounding factors affecting HRV, such as medication use, lifestyle factors, and physiological variability, could not be fully controlled.

These findings support the integration of group supportive psychotherapy into routine hemodialysis care as a feasible and low-cost adjunctive intervention. Incorporating structured psychosocial support may enhance patient-

centered care, improve quality of life, and address unmet psychological needs in ESRD populations. This approach aligns with the biopsychosocial model and may be particularly valuable in resource-limited settings.

CONCLUSION

Group supportive psychotherapy significantly improves quality of life and increases plasma serotonin levels in ESRD patients undergoing chronic hemodialysis. No statistically significant changes in HRV were observed.

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CONFLICT OF INTEREST

There is no conflict of interest.

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