



The Effects of Exercise and Reminiscence Therapy on Depression and Quality of Life Among the Older Adults with Mild Alzheimer's Disease

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ABSTRACT

Alzheimer's disease (AD) is the most common cause of dementia in older adults. Depression is an important co-morbid disorder in this group, as it may decrease their quality of life (QoL). Exercise or Reminiscence therapy (RT) is thought to be viable in lessening the degree of depression in older adults. To investigate and compare the impacts of integrated exercise and reminiscence therapy on depression level and QoL in older adults. A single-blinded quasi-experimental study with a comparison group design was conducted on 51 institutionalized older adults with mild-to-moderate AD and were grouped into (i) Reminiscence (RT, n = 17), (ii) exercise (EX, n = 16), and (iii) exercise coupled with Reminiscence (ER, n = 18). The depression level was assessed using the Cornell Scale for Depression in Dementia (CSDD); the QoL was assessed using the QOL-AD scale. A repeated-measures ANOVA was used for data analyses. Results: The reminiscence therapy alone or in combination with the exercise was effective in reducing depression levels and improved QoL in the older adults ($p < .05$). The reminiscence therapy alone or in combination with the exercise was effective in reducing depression levels and improved QoL in older adults. This study found significant improvements in the mean score of CSDD and QOL-AD of the ER, thus supporting its effectiveness in reducing depressive symptoms and improving QoL in mild AD. These results help as a contribute to the healthcare practices to deliver an integrated reminiscence and exercise in older adults' rehabilitation.

1. Introduction

The most widely recognized neurodegenerative disorder among the older adults is Alzheimer's disease (AD). As per the World Alzheimer Report delivered by Alzheimer's Disease International, more than 50 million individuals are affected by the AD and is projected the number are to increase more than triple by 2050 [1]. According to the National Institute of Aging (NIA) among people with Alzheimer's disease, 50.4% had mild disease, 30.3% had moderate disease, and 19.3% had severe disease [2]. In Malaysia, the prevalence is 14.3%, which is relatively higher compared to other countries, this includes all the stages of AD [3]. AD among older adults may lead to the impairment

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of cognitive and motor functions and the development of nonmotor disorders, such as depression. It is estimated that about 87% of the older adults with AD are depressed [5]. Moreover, depression and cognitive impairment are identified as independent factors influencing the quality of life among the elderly [4]. Perhaps, the prevalence of AD is higher in older adults living in long-term care institutions than those living in general communities [5].

Previously, Siverová and Bužgová [6], in 2018, revealed that those older adults who were lonely and socially isolated were associated with higher rates of depression which in turn results in low physical activity engagement and poor QoL. In addition, the older adult with greater depressive symptoms could have dysfunctional social behavior which results in them thinking and reacting differently. It remains unknown, and this situation is rarely noticed because it is very rarely reported. Depressed older adult with AD have been described in literature before, but investigations in the low- and middle-income countries, including Malaysia, are limited. In institutionalized patients with AD, only one study has identified the prevalence of depression which are 41% and 29% of patients, experiencing moderate and extreme depression, respectively [7]. However, there is no convincing evidence that shows depression as a factor for developing the outcomes of QoL amongst this population.

Current systematic review revealed that regular light physical exercise especially in the morning, sporting activities at leisure time, and a wide variety of exercises, at least three times a week, high intensity, could benefit overall physical health and quality of life of older adults [8]. Similarly, a meta-analysis and systematic review has reported that exercise is cost-effective in enhancing cognition and reducing depressive symptoms in the older adult with and without AD [9,10]. Also, aerobic training conducted for 12 to 24 weeks, has a significant effect on cognition and depression [11]. However, whether the immediate effects of exercise training can be beneficial in improving moods or depressive symptoms among mild AD remained inconclusive. An older adult with AD usually tends to behave differently due to communication dysfunction and psychomotor impairment. The implementation of reminiscence therapy (RT) is shown to have promising results for older adult with depression and mild to severe impairment of cognition [12].

The reminiscence therapy (RT) is a nonpharmacological technique that increases the self-esteem and brings a feeling of happiness and relaxation to older adults as they look back on their lives [13]. Besides, this technique is unique as it may be conducted in a formal, informal, one-on-one, or in a group setting. The RT normally involves recalling past events, thereby encouraging older adults to communicate and interact with listeners or respondents [14]. Older adults can have deep-rooted episodic memories of past events stimulated and remember by using old music, photographs, and film thus enhancing recall from long-term memory. A study has reported that as early as four weeks of RT can effectively reduce depressive symptoms among institutionalized older males [15].

Also, an integrated exercise and RT seems to bring superior effects, compared to one intervention alone to improve the depression level in the older adults. As further claimed by Yujia *et al.*, [16] that 8-week of physical exercise combined with group reminiscence could improve on spiritual well-being of the older adults after the outbreak of the COVID-19 epidemic. Strongly supported by latest systematic review on the effect of repeated-measured design on the combined effect of physical exercise, music, and cognitive intervention on cognitive function for older with AD are recommended [17].

However, majority of previous studies have described the utilization of exercise and the RT for the older adult separately [18,19]. In Malaysia, multiple races with different cultures and beliefs exist, and the diversity in reminiscence approaches results in difficulty in comparison. Thus, the effects of the exercise combined with the RT may vary. To some extent, the combination of group exercise and the RT can be more beneficial for the older adult compared with separate interventions because the

benefit of the exercise alone or RT alone may be expected to reinforce the benefit of the intervention. Therefore, the objective for this study is to investigate the effect of the exercise combination RT on the level of depression and the QOL of older adult with AD.

2. Methodology

2.1 Study Design

The current study used a quasi-experiment with a comparison group design. The difference in differences (DID) was used to identify the impact of an intervention on the people in sites where the intervention is implemented. DID is achieved by comparing changes in outcomes over time for the intervention group and control group.

2.2 Sample

Respondents from the Rumah Seri Kenangan Cheras was chosen and had been invited to voluntarily participate in this study. The total number of 51 older adults aged above 60 years were recruited and expected to provide significant effects from the intervention in this study. Three participants were excluded from the data analysis due to not coming to intervention classes more than two times. The reasons for study drop out were not in good health. The respondents were included if they met the criteria as follows; (i) the older adult aged 60 years or above, been diagnosed with AD by a neurologist, (ii) had been living in the institution for at least three months, (iii) had mild to moderate AD as determined by the baseline Montreal cognitive assessment (MoCA) score $> 19-25$ (iv) the value of the Geriatric Depression Scale (GDS) ≥ 11 and (v) signed informed consent form [20]. Respondents who were bedridden or in a wheelchair were excluded from the analysis. Both respondents and their caregivers or their legal guardians have given written consent.

2.3 Instruments

A demographic questionnaire was used to measure the data consisting of age, gender, educational status, marriage, employment, and health status. The level of depression in the older adult as measure by using the 19-item Cornell Scale for Depression in Dementia (CSDD) [21]. The questionnaire analyzed an individual's mood-related outcomes, physical observations, behavioral shifts, cyclic roles, and intellectual changes. The scale was ordered by the researcher to the respondents separately in a semi-structured interview format in the Malay edition. Each question was scored from 0 to 2: 0, absent; 1, mild or intermittent; and 2, severe. Not applicable represented an inability to evaluate. Depression was detected if a score ≥ 11 . Cornell Scale for Depression had showed high interrater reliability with Cronbach's alpha 0.84 which is high correlations with the Geriatric Depression Scale (0.82), and excellent sensitivity (0.93) and specificity (0.97) at a cutoff of 6 in a mixed dementia and normal older adult population [21]. Besides, the CSDD is reliable and valid for diagnosing depression in dementia in A demographic questionnaire was used to measure the data consisting of age, gender, educational status, marriage, employment, and health status. The level of depression in the older adult as measure by using the 19-item Cornell Scale for Depression in Dementia (CSDD) older Turkish adults. This can be seen with a high test-retest correlation level ($r: 0.93$) was obtained for the total scores of the scale with high internal consistency ($\alpha: 0.86$), among demented older adults with and without depression [22].

The QoL was measured by using the EUROHIS-QOL. The WHO-8 is a short quality of life measure that was derived from the original WHOQOL100 and the WHOQOL-BREF [23]. It contains of eight

items which are demonstrative of two items from each of the physical, psychological, social, and environmental domains of the WHOQOL-BREF [23]. EUROHIS-QOL demonstrated good internal consistency, with an alpha ranging from 0.80 to 0.83; low to moderate floor and ceiling effects among the adult patients (age 18 years and above) and healthy adults in Brazil [24]. The reliability internal consistency was measure using Cronbach's alpha coefficient.

2.4 Intervention

The current study involved three groups, namely, the RT only (RT, $n = 17$), exercise only (EX, $n = 16$), and exercise coupled with the RT (ER, $n = 18$). For six weeks, the respondent in ER received group exercise and individualized RT, whereas respondents in the EX and RT received only group exercise and individualized RT, respectively. The researcher completed the training for the ER group first followed by concurrent training for the EX and the RT groups.

2.4.1 Exercise training

The purpose of the exercise training was to enable respondents to perform at least 150 minutes of physical activity of moderate intensity each week [25]. The respondents were asked to complete a 60-minute session three times per week. The group-based exercise training was adapted from a previous study with modifications for the type of movements, speed, and exercise volume [26]. The exercise training was conducted every Tuesday, Thursday, and Saturday (8:00 a.m. to 9:00 a.m.) for six weeks, resulting in a total of 18 sessions. This training exercise was built on the basis of four fitness aspects and involves cardiovascular endurance, strength of the muscles, balance, locomotor and flexibility exercise. The key aim was to include all the body's major muscle groups. Two qualified physiotherapists were appointed to lead the exercise groups. The researcher supervised the sessions. The sessions were also combined with music to keep the respondents motivated [27]. This exercise training complied with the American College of Sports Medicine's guideline that exercise training for older people should be performed for 1 hour on alternating days to reduce long sessions and avoid fatigue and risk of injury [18].

2.4.2 Individualized RT

For following six weeks, an individualized RT with one session per week was held and continued after the cessation of the physical exercise, which lasted for 40–60 minutes. The topics for the RT were chosen on the basis of the recommendations by Siverová and Bužgová [6]. The respondents were asked at each session to remember their memories on particular topics, including specific respondents such as (1) the place where I come from during childhood; (2) favorite activities and games during childhood; (3) school years, teachers, schoolmates, and friends; (4) first love, first date, early marriage, and memorable anniversary; (5) favorite meals and dining; (6) holiday or festivities, such as Hari Raya, Chinese New Year, and Deepavali and discuss the food during all the celebrations. All sessions were conducted by the lead researcher and assisted by two occupational therapists. The researcher attended the RT courses and have certificates of competency to run the RT techniques and work. At the beginning of each session, the therapist introduced the respondent and invited them to share their memories and stories about past events or their experiences interactively. Specific questions were supported and answered by the therapist. Objects of reminiscence, such as taking photographs, video tapes, songs, and cuisines, were used as stimuli to help the respondents recall and share their stories. Refreshments, including cookies, bread, and drinks, were also offered

by the therapist. When the counseling period ended, the therapist closed the session for each week with a summary focused on the topic. In the following week, the respondent was then addressed with a 'see you next week' closing message by the therapist. Table 1 shows the RT activities.

Table 1
 Reminiscence Therapy Activities

Week / Themes	Contents	Expected Outcomes
Week-1: "The place where I come from during childhood."	Introduction and orientation (draw a house-tree-person) with crayons Recall positive memories	<ul style="list-style-type: none"> ● To confirm one identity ● To restore peace of mind
Week-2: "Favorite activities and games during childhood"	The happiness of childhood games – recall and use multimedia technology (graphics, text, video, and sounds)	<ul style="list-style-type: none"> ● To increase personal self-esteem and motivation ● To increase awareness and time
Week-3 "School years, teachers, schoolmates, and friends."	Recall positive memories about schools, teachers, schoolmates, and friends. Depict a very lovable person by using paper and clay	<ul style="list-style-type: none"> ● To obtain psychological support and improved self-integration ● To provide relaxation and peace
Week-4: "First loves, first dating, early marriage, memorable anniversary."	Depict a very lovable person by using paper and clay Express the feeling of that time (photography)	<ul style="list-style-type: none"> ● To obtain psychological support and improved self-integration ● To improve self-reliance
Week-5: "Favorite meals and dining."	Share their favorite meals and dining – express using hand activities such as putty, clay, or colored papers.	<ul style="list-style-type: none"> ● To increase personal self-esteem and motivation ● To improve muscle strengths and coordination

2.5 Data Collection and Analysis

This study was conducted in the Rumah Seri Kenangan, Cheras from February to September 2021. The data was collected by the researchers themselves, with the help of four research assistants. Each assistant was taught how to intervene and gather data with the help of a questionnaire and performance-based outcome measures. The analytical research was conducted using version 22.0.0. of SPSS. Descriptive statistics were calculated including counts and percentages for categorical variables and means and standard deviations for continuous variables. Mixed ANOVA tests were conducted to compare scores among the three groups on depression and QoL at baseline, 3rd week, and 6th week. The level of significance was set at $p < 0.05$.

2.6 Ethical Consideration

This study was conducted in line with the Helsinki Declaration and the protocol was approved by the Institution Research Ethics Committee (Reference No. 600-IRMI [5/1/6]).

3. Results and Discussion

For the characteristics of the respondent in this study, findings shows the average age of respondents in the RT was 71 years, in the EX groups was 70 years and in the ER group was 68 years. A total of 51.0% of the sample were women, 52.9% were never married, 52.9% had primary level in education, and 56.8% did not exercise. There was no significant difference in the respondents' characteristics between the three groups group ($p > .05$). See Table 2.

Table 2
 Demographic Characteristics and Medications Status of Respondents

Characteristic	RT group		EX group		ER group		F test (p-value)
	n(%)	M(SD)	n(%)	M(SD)	n(%)	M(SD)	
Age		71.76 (7.16)		70.00 (6.84)		68.06 (5.43)	F=1.429 0.250
Gender							0.293
Male	6(35.3)		10(62.5)		9(50.0)		
Female	11(64.7)		6(37.5)		9(50.0)		
Smoking							0.537
Yes	3(17.6)		2(12.5)		1(5.6)		
No	14(82.4)		14(87.5)		17(94.4)		
Marital status							0.208
Never	6(35.3)		8(50.0)		13(72.2)		
Married	1(5.9)		-		2(11.1)		
Divorced/separated	5(29.4)		4(25.0)		1(5.6)		
Death of spouse	5(29.4)		4(25.0)		2(11.1)		
Education							0.391
None	1(5.9)		1(6.3)		2(11.1)		
primary	9(52.9)		7(43.8)		11(61.9)		
Secondary	5(29.4)		8(50.0)		5(27.8)		
tertiary	2(11.8)		-		-		
Exercise status							0.605
No	8(47.1)		10(62.5)		11(61.1)		
Yes	9(52.9)		6(37.5)		7(38.9)		

* ^aChi-Square ^bIndependent

Table 3 and Figure 1 show the depression level scores between all groups at baseline, 3rd and 6th weeks. A 3 x 3 mixed-model ANOVA was used to investigate the impact of combined interventions on the depressions level in older adult with mild AD. A significant main effect for time was obtained $F(2, 96) = 30.382, p < .001$, partial $\eta^2 = .38$ with depression scores after the intervention ($M = 6.86, SD = 1.833$) being significantly lower than before the intervention ($M = 8.61, SD = 0.896$). A non-significant main effect between group was found, $F(2, 48) = 0.039, p = .962$, partial $\eta^2 = .02$. Post-hoc comparisons using the Bonferroni test showed non-significant mean differences ($p < 0.05$) for depression among all groups (RO and EO = 0.40; RO and ER = 0.09; EO and ER = 0.31). Also, a non-significant interaction between time and group was reported, $F(4, 96) = 0.086, p = .987$, partial $\eta^2 = .004$.

Table 3

Mixed Model ANOVA for Depression Scores between all groups at baseline, 3rd and 6th weeks

Time / Groups	n	Baseline Mean ± SD	3 rd Week Mean ± SD	6 th Week Mean ± SD	% Changes (sec)	Mix ANOVA Outcomes
RO	17	8.76 ± 1.091	8.12 ± 0.993	6.94 ± 1.435	20.78	Time: F (2, 96) =30.382, p < .001, partial η ² =.38 Group: F (2, 48) = 0.039, p = .962, partial η ² =.02 Time x Group: F (4, 96) = 0.086, p = .987, partial η ² =.004
EO	16	8.31 ± 0.602	7.63 ± 1.088	6.69 ± 2.774	19.49	
ER	18	8.72 ± 0.895	7.89 ± 1.023	6.94 ± 1.056	20.41	

Note: Data are presented as mean ± SD. *The mean difference is significant at the level of p < 0.05

RO = Reminiscence only; EO = Exercise Only; ER = Exercise and Reminiscence ; SD = Standard Deviation ; % = Percentage of changes

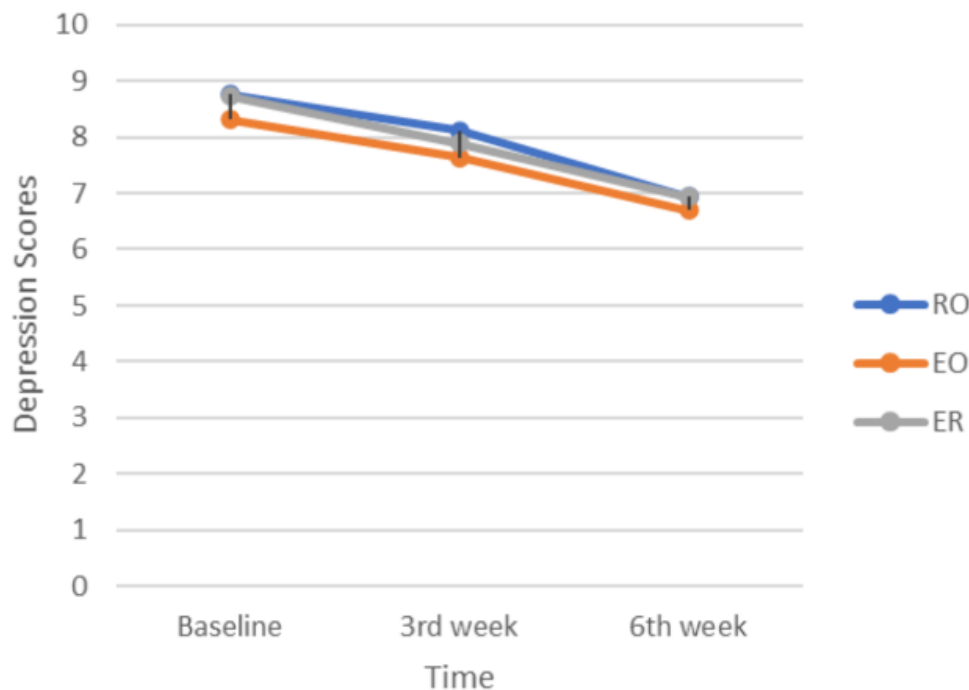


Fig. 1. The changes of depression scores for all groups in term of mean differences at baseline, 3rd and 6th weeks

Table 4 and Figure 2 show a significant main effect for time was obtained F (2, 96) =9.038, p < .001, partial η² =.158 with quality-of-life levels after the intervention as (M = 27.84, SD = 3.264) being significantly higher than before the intervention (M = 26.03, SD = 4.52). A non-significant main effect for between group was found, F (2, 48) = 0.039, p = .962, partial η² =.02. Post-hoc comparisons using the Bonferroni test showed significant mean differences (p < 0.05) for quality of life among all groups (RO and EO = 0.98; RO and ER = 1.22; EO and ER = 0.24). Also, a non-significant interaction between time and group was reported, F (4, 96) = 0.086, p = .987, partial η²=.004.

Table 4

Mixed Model ANOVA for Quality of life level between all groups at baseline, 3rd and 6th weeks

Time/ Groups	n	Baseline			3 rd Week			6 th Week			% Changes (sec)	Mix ANOVA Outcomes
		Mean ± SD	±	Mean ± SD	±	Mean ± SD	±	Mean ± SD	±			
RO	17	27.47	±	27.47	±	28.00	±	1.93	Time: F (2, 96) =30.382, p < .001, partial η ² =.38 Group: F (2, 48) = 0.039, p = .962, partial η ² =.02 Time x Group: F (4, 96) = 0.086, p = .987, partial η ² =.004			
		3.986		4.155		3.622						
EO	16	25.56	±	27.00	±	27.43	±	7.32				
		4.966		±3.777		3.669						
ER	18	25.11	±	26.11	±	28.055	±	11.73				
		4.496		±4.100		2.622						

Note: Data are presented as mean ± SD. *The mean difference is significant at the level of p < 0.05

RO =Reminiscence only; EO= Exercise Only ; ER = Exercise and Reminiscence ; SD= Standard Deviation ; %= Percentage of change

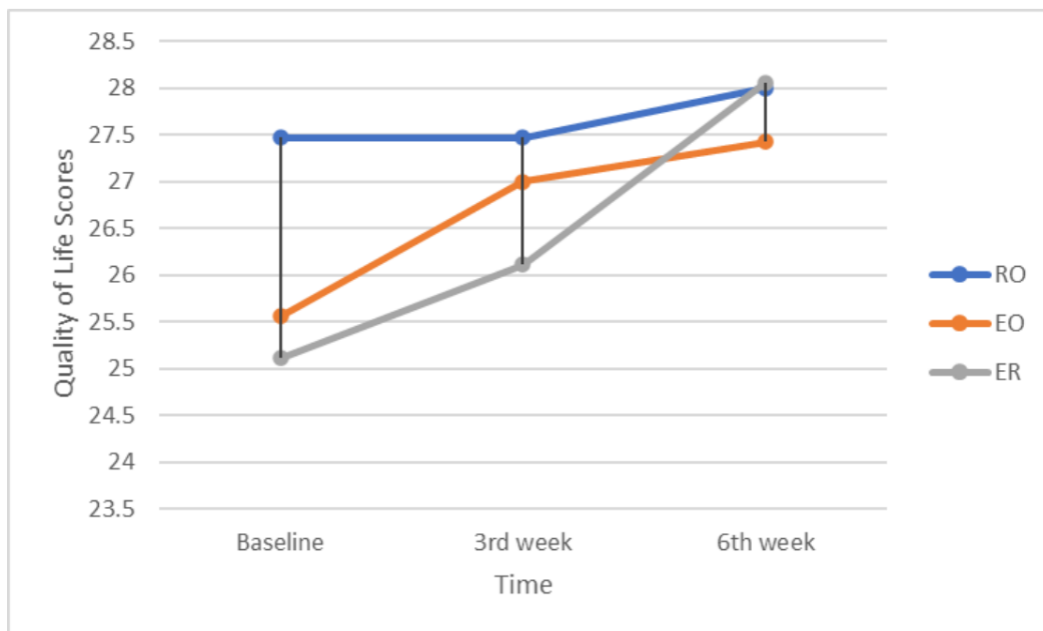


Fig. 2. The changes of quality of life scores for all groups in term of mean differences at baseline, 3rd and 6th weeks

Latest findings from the regression analysis reported that those with never-married older adults significantly direct related to depressive symptoms, comparing with married individuals [28]. This never-married older adults typically had longer periods of loneliness, fewer social support, and lower self-esteem, thus they may have increased their risk of depression. Besides, majority of the respondents also presented with primary or low education status. It is further supported by previous qualitative meta-analysis findings that less education is associated with increased risk of late life depression among older adults [29]. It is believed that depressive symptoms are linked to educational attainment, and it can be influenced by a variety of socioeconomic factors. There is no easy way to boost a country's health and economic success at lower levels of education status or achievement.

This study shows that the combined exercise training and RT for six weeks may reduce the level of depression and improve the QoL. The respondents in the ER group have improved CSSD scores following the completion of interventions. Exercise provides psychological advantages without the risks or costs of substance treatment to relieve depression, which is believed to be due to several

mechanisms that may be operating simultaneously. First, the decline in symptoms of depression is attributed to an increase in core body temperature after exercise. Increased body temperature especially at the brain stem leads to an overall feeling of relaxation and reduction in muscular tension as proposed in the thermogenic hypothesis [30,31]. Second, the endorphin hypothesis indicates that exercise has a beneficial impact on depression as a consequence of increased release during exercise of β -endorphins. A good mood and an overall increased sense of well-being for older adult are correlated with endorphins. The respondents in the ER who have received both interventions may benefit from the combined exercise and RT due to the improved sense of wellbeing. This finding is supported by a previous review that has discussed that the hormone modulation may affect the hippocampal plasticity even in older adult with AD because the hippocampus plays a central role in the cognition and mood regulations [32]. These improvements tend to play an important role in the development of exercise-induced neurogenesis and memory, which are essential for reducing depressive symptoms.

There is also a slight improvement in the percentage of changes after the termination of the intervention. The respondent in the RO and ER received the reminiscence therapy in their course. The older adult were guided to evaluate, re-experience, and produce fresh interpretations of their former lives in order to assist them better understand themselves, boost self-esteem, and promote socializing in this present study [33]. The added value of the reminiscence therapy had been administered by reminiscence therapy in a group setting according to the needs of the participants. Furthermore, a researcher already divided the reminiscence therapy into simple reminiscence suggested by Gil *et al.*, [34]. The study suggested that this intervention is more practical and suitable for the older adults with minor psychological issues who do not require medication intervention.

Each respondent believed in themselves after the termination of program as reminiscence enhance their level of confidence about their life [35]. It was believed that reminiscing about memorable and joyful events can promote positive moods and minimize the release of stress chemicals such as cortisol in a person [26]. Perhaps, individuals are also given a sense of enjoyment and a good environment. In addition, reminiscence activities, especially in group-based approaches can help people with Alzheimer's disease to improve their communication and social activities. This is because interacting with another person can relieve their psychological burden and stress by remembering about pleasant occurrences, which activates the neural circuit, particularly in the striatum, and boosts positive mood and happiness [36,37].

The current finding is consistent with a prior study that found that, their interactions with the therapist improved, and they were more engaged during the activity provided in the intervention, as seen by an increase in the degree of engagement after three weeks [36]. Lopes and his colleagues have demonstrated that reminiscence therapy can benefit cognitive function maintenance or improvement, anxiety reduction, and the management of depressive symptoms and altered behavior [38]. The respondents in the ER group have received the RT as part of these interventions and have shown consistent positive attitudes and behavior. Each respondent believes in themselves after the termination of the program as RT enhances their level of confidence. RT is claimed to offer people a sense of satisfaction and a good atmosphere and increase communication and social engagement among older adults with AD [39]. The current finding is in agreement with the results of Tsai and his colleagues, which show that their interactions with the therapist have improved and that the respondents are approachable during the activity given in the intervention [40]. These phenomena may result in improved socialization and induced feelings of accomplishment in respondents, all of which assist in reducing depression.

The respondents in the EX group show little changes in reducing the symptoms of depression and the QoL. This could be due to the acute effect of aerobic exercise in the insulin-like growth factor-1

(IGF-1) circulating plasma level [40]. In addition, Tsai and his colleagues have reported that exercise affects the brain by circulating growth factors that cross the blood barrier and modulate many cognitive pathways, including neurotrophic brain factor, IGF-1, and endothelial vascular growth factor for brain health [40]. The respondents in this group have received exercise training but have not received the RT after the termination of the training. The continuity and the long-term engagement in exercise are believed to be needed to gain its significant health benefits. The respondents may have several barriers to engage in exercise or demotivated, thus resulting in poor exercise adherence.

No significant difference is observed in the respondents in the RT, but a declining trend in the depression symptoms is seen. The RT is prescribed as an effective depression medication and has been shown to improve cognitive and emotional functions in older adults with AD. The respondents in this group may have intentions or goals to start active participation in an exercise or any physical activity to combat their depression but may not know how to proceed. The introduction to exercising and continuing education for older adults with cognitive impairments seem important to be integrated as a practical session [32]. Therefore, exercise training should be included as part of the daily routine because older adults with AD experience progressive loss of independent functioning, which may lead to reduced overall QOL. It is also believed that be des older adults, those younger generations suffered from low self-esteem and social appearance anxiety in the context of self-editing on social media [41]. It can be suggested that part of Reminiscence therapy could help influencing both self-esteem and social appearance anxiety, thus reduce the risk of adverse psychological well-being.

4. Conclusions

There are several limitations from this study. The respondents were multi-races, thus the results could lead to bias. The main objective of RT is to increase the participants' sense of empowerment and to carry out an appropriate life review that would enable the growth of wholeness. The majority of respondents have a variety of natural coping mechanisms to deal with the demands of daily life. However, in extremely stressful situations such as uncertainty and no sense of control, people tend to be institutionalized or are depressed. These circumstances may overwhelm coping mechanisms and prevent people from using their current behavioral repertoires. Respondents should receive RT in order to improve their coping skills and gain a fundamental understanding of their life circumstances.

Our results suggest that exercise training combined with RT may be superior in improving the depression level and QOL compared with RT or exercise alone. Thus, this integrates interventions may be recommended as a routine activity for older adults living in institutions, particularly those with cognitive impairments. Duplication of this analysis using large samples drawn from various populations and extended durations is recommended for further assessment to confirm the significance of the findings.

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