Home-Based Computerized Cognitive Training for Postoperative Cognitive Dysfunction After Lung Transplantation in Elderly Population

A Randomized Controlled Trial

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Abstract: Postoperative cognitive dysfunction is a severe outcome after lung transplantation, especially in the elderly lung transplant recipients. Home-based computerized cognitive training (CCT) is a widely used intervention for cognition improvement, but its efficacy has not been validated in this population. A randomized controlled trial was conducted to analyze the effect of CCT on elderly lung transplant recipients. The participants received either an 8-week CCT intervention or usual care. The changes of cognitive function were assessed between preintervention (T1), postintervention (T2), and 12 weeks postintervention (T3). Among the 46 participants, 91.3% completed the interventions. The CCT group performed better than the control group on Digit-Span Forward Test (T3: $p = 0.0044$) and Verbal Fluency Test (T3: $p = 0.0331$), indicating the efficacy of CCT on verbal memory in the elderly lung transplant recipients. Although varied impacts were observed on different cognitive domains, it seems promising to use CCT on the elderly population after lung transplantation.

Key Words: Home-based computerized cognitive training, neurocognitive impairment, lung transplantation, postoperative cognitive dysfunction

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Lung transplantation remains as the final option for patients with end-stage lung diseases. With an aging population, the developed surgical techniques, and the mended Lung Allocation Score, the median recipient age of the lung transplant keeps growing and approached age 56 years in 2011 as reported by the International Society of Heart and Lung Transplantation (ISHLT) (Hoffman et al., 2012). Currently, neurocognitive impairment is an important problem among lung transplant recipients. Postoperative cognitive dysfunction (POCD) associated with solid organ transplantation is common in the elderly patients, and preoperative neurocognitive impairment is prevalent as a consequence of advanced pulmonary diseases (Hoffman et al., 2012; Smith et al., 2014). It has been reported that POCD is prevalent in 29% to 57% patients after lung transplantation and affects various domains of cognitive function (Hoffman et al., 2012; Smith et al., 2018; Smith et al., 2014). Impaired neurocognitive function will negatively affect the quality of life of the patients and the following medication adherence, which was also shown to be associated with lower posttransplant survival (Hoffman et al., 2012; Skvarc et al., 2018). Therefore, it becomes imperative to develop a strategy to combat the neurocognitive deficits among the lung transplant recipients.

Although pharmaceutical treatments are available for delaying or alleviating POCD (Skvarc et al., 2018; Wang et al., 2017; Zhang et al., 2018), lifestyle interventions, for example, nutrition, exercise, and cognitive training, are considered to have less adverse effects (Hill et al., 2017; Ten Brinke et al., 2017; Winger et al., 2018). In recent years, there is growing interest in computerized cognitive training (CCT), which comprises a series of cognitively challenging activities such as attention, memory, and executive function training (Kalbe et al., 2018; Ten Brinke et al., 2017). CCT is more convenient and inexpensive than the supervised cognitive training as it is based on individuals' electronic devices, for example, computers or tablets (Ten Brinke et al., 2017), making it easy to promote and administer. Current evidence suggests that CCT provides multidimensional benefits for the cognitive function of the aging people, such as in verbal and nonverbal memory, working memory, attention, visuospatial ability, and processing speed (Hill et al., 2017; Ten Brinke et al., 2017). A randomized controlled trial also demonstrated that the CCT-corrected cognitive function remains higher than the baseline after 1 year postintervention (Lampit et al., 2014).

Although CCT has been proved beneficial across populations with various healthy conditions or multiple medical standards (Conklin et al., 2015; Elgamal et al., 2007; Hill et al., 2017; Kalbe et al., 2018; Ten Brinke et al., 2017; Wu et al., 2018), the effect of CCT on the elderly population among lung transplant recipients has not been investigated. The present study conducted a randomized controlled trial to examine the feasibility of applying home-based CCT among lung transplant recipients and investigate its effect on improving the cognitive function of the elderly patients after the lung transplantation. It was hypothesized that (1) more than 50% of eligible participants would agree to be randomized and less than 70% would complete the study, and (2) CCT would improve the basic level of cognitive performance more than usual care (the control group).

METHODS

Participants

This study consisted of elderly lung transplant recipients aged older than 55 years who underwent the surgery with general anesthesia. The candidates were enrolled from Shanxian Central Hospital between May 2017 and September 2018. The candidates were screened by the inclusion and exclusion criteria according to the previous study (Kalbe et al., 2018; Payne and Stine-Morrow, 2017; Ten Brinke et al., 2018; Wu et al., 2018). The potential participants should be Mandarin speakers and should have sufficiently good vision, hearing, and motor ability to accomplish electronic devices-based tasks. Meanwhile, the participants should have no history of neuropsychological diseases, for example, Alzheimer disease, Parkinson disease, schizophrenia, or psychiatric

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disorders, and should have not participated in any physical, social, or neuropsychological interventions in the past 3 years. Montreal Cognitive Assessment Battery (MoCA) and Mini Mental State Examination (MMSE) were used to exclude the patients with preoperative cognitive dysfunction (MoCA ≤26 points or MMSE <24/30 points). In this study, one extra score was reduced from the preoperative MoCA or MMSE score if the patient was educated for less than 12 years. Written informed consents were obtained before the screening of eligibility. All studies were approved by Shanxian Central Hospital.

Procedure of the Study

Lung transplant candidates were first contacted by phone or email 1 month before the transplant surgery, and patients who showed interest in this study were given information about the aim of the study, CCT, and the neuropsychological assessments, as well as the inclusion and exclusion criteria. The sociodemographic, physical, and neurocognitive data of the candidates were collected within 1 month before the surgery. After the screening for the eligibility of the participants, the participants were randomly allocated to receive either CCT intervention or the usual care. Equal numbers of patients were allocated to the CCT group and the control group. CCT intervention and the control intervention were not performed until 4 weeks after the surgery to allow for the recovery of the physical conditions of the patients. CCT and the control intervention lasted for 8 weeks. Neurocognitive assessments were conducted three times during the research: the first (T1) and the second (T2) assessments were conducted right before and after CCT or the control intervention. The third assessment (T3) was posttraining 12 weeks after the commencement of the intervention. The tests were conducted individually by a trained psychometrician.

Randomization and Blinding

The participants were randomly allocated (1:1) to the CCT group and the control group. Each participant was given a code from 1 to 46 according to the time of enrolment. Blocked randomization was conducted using an online software (www.randomization.com) with a block size of two. The allocation of the groups was not blinded to the participants or the investigator, because a placebo intervention was not used in the control group, the investigator had to inform the participants of their group allocations. However, the psychometrician was blinded to the group allocation when conducting the neurocognitive assessment to minimize the biases.

CCT and the Control Intervention

The CCT program administered in this study was based on Posit Science BrainHQ suite (Posit Science Inc, San Francisco, CA) (Woods et al., 2018). It consists eight exercises, among which four exercises aim at improving the attention and information processing speed, while the other four exercises train the working memory (Woods et al., 2018). The participants in the CCT group should practice four tasks per day for 10 minutes per task, 5 days per week over the 8-week intervention. The order of the tasks was predesigned to allow the participants to perform each task for a balanced amount of time over the 8-week intervention, also to prevent the performing of the same tasks each day. The tasks contain different levels of difficulty, and adaptive Bayesian algorithms would adjust the difficulty based on individuals' performance to optimize the cognitive challenge for each participant (Lee et al., 2016; Wu et al., 2018). CCT was Web-based and multiplatform-compatible. The participants could perform the training either during hospitalization or at home by themselves. A homework calendar was provided to each participant to remind them of the training and promote the training adherence as well (Ten Brinke et al., 2018). The registered training time per day was recorded by the program and monitored by the research team. During the intervention time course, participants in the control group retained their usual lifestyle, as a meta-analysis reviewed that there was no bias between passive control and placebo regarding the changes in the cognitive function (Hill et al., 2017; Kulason et al., 2018).

Cognitive Function Assessments

During the screening of the eligibility, MoCA and MMSE were used to identify the preoperative cognitive-impaired candidates (Smith et al., 2014). Seven tests were administered to measure the change of a spectrum of the participants' cognitive functions over three time points: before intervention (T1), immediately after intervention (T2), and 12 weeks after the intervention (T3). In Digit-Span Forward Test and Digit-Span Backward Test, participants were required to repeat numbers with increasing span forward or backward immediately after they were read aloud by the examiner (Hoffman et al., 2012). In Verbal Fluency Test, participants should name all the words they can think of in a semantic or a phonetic category in 1 minute (Hoffman et al., 2012). In Trail Making Test A, participants were required to link the numbers on the paper from 1 to 25 in order correctly as quick as possible. In Trail Making Test B, participants should link the numbers and the letters alternately (1-A-2-B-3-C, etc.). These two tests measure the visuomotor attention, cognitive flexibility, and executive function (Hoffman et al., 2012; Smith et al., 2014). In Digit Symbol Test, participants were provided with nine pairs of number and symbol, and they were required to fit corresponding symbols to the blanks below a sequence of numbers within a minute, which would test the response speed, sustained attention, and visuospatial ability of the participants. In Word Recognition Test, participants were required to identify words in a list with no contextual help, which would assess the visual processing speed. In Trail Making Test A and B, a lower score indicates a better performance, whereas in other tests, a higher score indicates a better performance.

Statistical Analysis

This study was designed to evaluate the effect of CCT in the elderly population after lung transplantation. Social demographic, physical, and neuropsychological data of the experimental and the control group were compared using *t*-tests for independent samples to compare the age, years of education, body mass index (BMI), forced expiration volume (FEV_1), and overall cognitive function (MoCA and MMSE). The significance of the score changes in each test within the CCT group and the control group was determined by Wilcoxon signed-rank test (Kulason et al., 2018). The mean changes of the scores were calculated, and the significance values of changes between T2-T1, T3-T1, and T3-T2 were determined. An analysis of covariance (ANCOVA) with permutation test was conducted to determine the significance of the difference between the changes in the CCT group and the control group at both time points T2 and T3. The T2-T1 changes and T3-T1 changes were calculated. Factors such as sex, age, years of education, BMI, FEV_1, MoCA, and MMSE were evaluated as covariates during the ANCOVA analysis. Permutation test was conducted due to the small sample size to minimize the probability of type I error. One-tailed Wilcoxon signed-rank test and ANCOVA were used because it was hypothesized that CCT would improve the cognitive function. A significance of $\alpha = 0.05$ was set for all the analysis.

RESULTS

Process of the Study and the Feasibility of CCT

The graphical representation and the flow of participants are provided in Figure 1. A hundred transplant candidates were contacted, among whom 79 candidates responded to the enquiry. Among the 79 candidates, 11 refused to participate in the research, 17 did not meet the inclusion criteria, and 4 were unable to participate due to objective reasons. Thus, 47 participants were recruited to this research. The

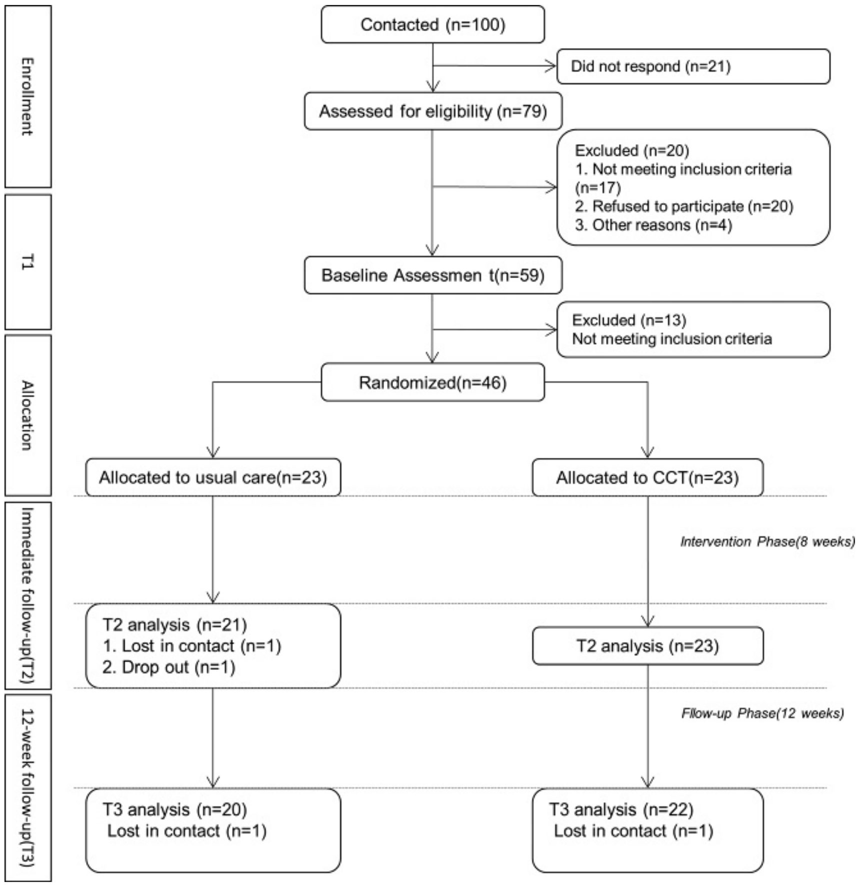

FIGURE 1. Design of the study and the participant flow. CCT indicates computerized cognitive training.

baseline cognitive performance of the participants was measured before the start of CCT (T1), after which one refused to participate. Hence, a total number of 46 participants were randomized and accepted CCT intervention or usual care (CCT: $n = 23$; control: $n = 23$). CCT started at the fifth week after the surgery, and CCT intervention lasted for 8 weeks. Outcome measurements occurred immediately after CCT process (T2) or equivalent in the control group, and 12 weeks after the end of the training (T3). Four people (8.7%) dropped out from the interventions (CCT: $n = 1$; control: $n = 3$) due to the loss of contact or their health condition. The data of 42 participants were used for statistical analysis (CCT: $n = 22$; control: $n = 20$). Overall, the hypothesis about feasibility was met (>50% agreed to be randomized; >70% completed the intervention).

Sociodemographic, Physical, and Neuropsychological Characteristics of the Participants

The sociodemographic, physical, and neuropsychological characteristics of the participants were measured before the lung transplant surgery (Table 1). Among the 46 participants, 30.4% were female, mostly married (97.8%), the mean age was 65.9 (SD = 5.5), the mean MMSE score was 25.8 (SD = 1.06), the mean MoCA score was 27.6 (SD = 2.12), and 82.6% were educated for 12 years or fewer. Their native diseases include chronic obstructive pulmonary diseases (COPDs) (41.3%), cystic fibrosis (23.9%), pulmonary fibrosis (15.2%), and others pulmonary diseases (8.7%). Participants of two sexes and with different native diseases were similarly distributed between the CCT group and the control group. There was no significant difference between the CCT group and the control group before the intervention with regard to age ($t = 1.262$, $p = 0.2208$), years of education ($t = 0.113$, $p = 0.9107$), BMI (kg/m^2) ($t = 10.59$, $p = 0.5613$), FEV_1 ($t = -1.639$, $p = 0.1151$), and overall cognitive state (MMSE: $t = -0.889$, $p = 0.3838$; MoCA: $t = -1.078$, $p = 0.2926$).

Changes in Neurocognitive Functioning Between Preintervention and Postintervention Within Groups

Neurocognitive testing occurred right before the intervention (T1), which was 4 weeks after the surgery, immediately after the intervention (T2), and 12 weeks after the intervention (T3) to assess the cognitive change within the CCT group and the control group. Outcome data of preintervention and postintervention performance in the CCT group and the control group were presented in Table 2. In the CCT group, analysis of the mean changes between the preintervention and postintervention scores in each test revealed significant improvement in Digit-Span Forward Test (T2: $p = 0.0116$, T3: $p = 0.0018$), Digit-Span Backward Test (T3: $p = 0.0032$), and Verbal Fluency Test (T3: $p = 0.0023$). In the control group, the outcome measurements were significantly higher in Digit-Span Backward Test (T3: $p = 0.0441$) as well. Noticeably, in the CCT group, the scores measured 12 weeks post-CCT (T3) were significantly higher than the scores measured right after CCT (T2) in Digit-Span Backward Test ($p = 0.0121$) and Verbal Fluency Test ($p = 0.0273$). However, the significance of the continued improvement after the intervention was not identified in any test in the control group. In both groups, fluctuated or even declined performance over the time course was observed in Trail Making Test A, Trail Making Test B, and Word Recognition Test, but these changes were not significant.

TABLE 1. Demographic and Background Information of Participants (n = 46)

	CCT Group (n = 23)		Control Group (n = 23)		All Participants (n = 46)	
Variable	**M (±SD)**	***n* (%)**	**M (±SD)**	***n* (%)**	**M (±SD)**	***n* (%)**
Sex						
Male		15		17		32
Female		8		6		14
Age	65.0 (±6.2)		66.8 (±4.7)		65.9 (±5.5)	
Education years						
<6		6		5		11
6–12		13		14		27
>12		4		4		8
Race/ethnicity	Chinese		Chinese		Chinese	
BMI, kg/m^2	20.9 (±1.01)		21.1 (±1.2)		21.1 (±1.1)	
Marital status						
Married/partnered		22		23		45
Divorced/separated		1		0		1
Native disease						
COPD		9		10		19
Cystic fibrosis		6		5		11
Pulmonary fibrosis		3		4		7
Other		3		2		5
FEV_1, L at 1 mo	2.52 (±0.16)		2.43 (±0.23)		2.47 (±0.20)	
MMSE	25.9 (±1.25)		25.7 (±0.95)		25.8 (±1.06)	
MoCA	27.9 (±2.39)		27.4 (±1.74)		27.6 (±2.12)	

TABLE 2. Comparison of Neuropsychological Tests Within Two Groups

Variable	Time Point	CCT Group (n = 22) M (±SD)	p	Control Group (n = 20) M (±SD)	p
Digit-Span Forward Test	Baseline	8.0 (±0.95)		8.8 (±1.8)	
	T2	8.6 (±0.79)	**0.0243***	8.8 (±1.11)	0.0696*
	T3	8.9 (±0.47)	**0.0006***/0.0556**	8.7 (±1.00)	0.5217*/0.7562**
Digit-Span Backward Test	Baseline	6.4 (±0.64)		6.3 (±1.49)	
	T2	6.6 (±0.58)	0.0874*	6.5 (±1.76)	0.1924*
	T3	6.8 (±0.46)	**0.0032*/0.0121***	6.6 (±1.45)	**0.0441***/0.4852**
Digit Symbol Test	Baseline	53.1 (±4.81)		53.2 (±5.44)	
	T2	53.7 (±4.53)	0.2297*	53.3 (±5.78)	0.5217*
	T3	53.7 (±4.76)	0.2611*/0.9095**	53.3 (±5.28)	0.7841*/0.9563**
Trail Making Test A	Baseline	31.0 (±4.43)		31.0 (±1.98)	
	T2	32.4 (±4.64)	0.2101*	31.1 (±2.39)	0.9482*
	T3	32.4 (±4.44)	0.0575*/0.7210**	31.4 (±2.57)	0.6849*/0.7210**
Trail Making Test B	Baseline	73.5 (±6.36)		69.9 (±7.19)	
	T2	73.2 (±6.36)	0.8202*	68.7 (±7.50)	0.2113*
	T3	74.3 (±5.91)	0.2360*/0.0696**	70.3 (±6.88)	0.5373*/0.1592**
Verbal Fluency Test	Baseline	14.5 (±2.35)		14.6 (±1.80)	
	T2	15.4 (±1.60)	0.0945*	14.9 (±1.49)	0.2173*
	T3	15.8 (±1.75)	**0.0023*/0.0273***	15.2 (±2.04)	0.3382*/0.9308**
Word Recognition Test	Baseline	9.3 (±0.90)		9.1 (±1.41)	
	T2	9.1 (±0.99)	0.211*	9.2 (±1.30)	0.5161*
	T3	9.4 (±1.21)	0.6495*/0.2443**	9.0 (±1.47)	0.3807*/0.3142**

Note: The significance level was set at $p < 0.05$.
Values in boldface indicate p values less than 0.05.
*p-value of T2 or T3 versus baseline.
**p-value of T3 versus T2.

Comparison Between the Effect of CCT and Usual Care

To check the benefits of CCT intervention on cognitive function compared with the control group, we conducted an ANCOVA with permutation test to evaluate the differences between the changing in scores in the CCT group and the control group. Comparison between preintervention and postintervention changes in the CCT group and the control group was presented in Table 3. The analysis of the differences between groups revealed no significant results in the intermediate measurements after the intervention (T2). However, the measurements taken 12 weeks after the intervention (T3) revealed significantly higher scores in the CCT group in Digit-Span Forward Test ($p = 0.0044$) and Verbal Fluency Test ($p = 0.0331$), indicating that the participants in the CCT group improved more in these two tests. Moreover, on a descriptive level, the changes in the CCT group seemed to be greater than the changes in the control group at both immediately after intervention (T2) and 12 weeks later (T3), although not all the differences were significant.

DISCUSSION

POCD is a severe outcome of lung transplant surgeries, which will negatively affect the medication adherence and the life quality of the patients. The severity of POCD seems to be correlated with the older age of the patients, and in recent years, the median age of the lung transplant recipients has constantly increased (Hoffman et al., 2012). With a large and growing basal number of the aging people, the treatment of POCD in this population is of great importance. CCT, as a lifestyle intervention, is cheap and easy to administer and has less adverse effects than the pharmaceutical therapies. CCT was able to improve the overall cognitive function in the potentially or mildly cognitive-impaired patients (Kalbe et al., 2018; Lampit et al., 2014; Wu et al., 2018), but the efficacy of CCT among the elderly POCD population have not been validated yet.

This study aimed to examine the effect of CCT on combating neurocognitive decline after lung transplantation in the elderly population. In this randomized controlled trial, seven neurocognitive tests were used to measure the CCT outcome, and significant effects were demonstrated in the CCT group in the Digit-Span Forward Test and Verbal Fluency Test compared with the control group (Table 3). Although significant changes were observed regarding the test scores, there are no standards for the transfer between each test and the corresponding cognitive domain. In different studies, Digit-Span Tests were considered to represent verbal memory (Hoffman et al., 2012), working memory (Kesse-Guyot et al., 2011), executive function (Kesler et al., 2013; Smith et al., 2018), or attention (Boone et al., 2007), and Verbal Fluency Test were considered to represent verbal memory (Smith et al., 2018), executive function (Hoffman et al., 2012; Kalbe et al., 2018; Kesler et al., 2013; Shao et al., 2014), or language (Boone et al., 2007; Shao et al., 2014), respectively. According to Kesse-Guyot et al. (2011) and Smith et al. (2018), both tests were affected by more than one cognitive domain, and in their analysis, Verbal Fluency Test reflects more of verbal memory, whereas Digit-Span Tests reflect more of the executive functioning. Here, this relation between tests and cognitive domains was accepted, and the results suggested that CCT improved the verbal memory in the elderly population after lung transplantation and might have improved their executive functioning in some extent. Despite the pattern used to transfer tests scores and cognitive domains, the significant differences between the CCT group and the control group indicate the efficacy of CCT on improving cognitive performance in some respects in the target population.

It is also interesting to notice that the significant differences between the CCT group and the control group occurred not immediately after the intervention but 12 weeks later. In those tests, the performance in the CCT group kept improving after the end of CCT, but this trend was not observed in the control group. To our knowledge, the continued cognition enhancing was barely noted in other studies of CCT. In a longitudinal research involving elderly people with dementia risk factors, although the impacts of CCT persisted 12 weeks postintervention, the scores for memory, executive function, and global cognition peaked at the end of CCT and declined post-CCT (Lampit et al., 2014). In a study of using CCT on cancer-related cognitive impairment among adults, the improvement of verbal memory and visual memory did not sustain 8 weeks postintervention (Wu et al., 2018). However, in a study involving teenager cancer survivor, the overall cognitive performance kept increasing 12 weeks post-CCT (Hardy et al., 2011). This contradiction on the long-term effect of CCT might due to the varied demographic and medical characteristics of the participants between different studies, or

TABLE 3. Comparison of Neuropsychological Tests Between Two Groups

Variable	Time Point	CCT Group Δ in Score	Control Group Δ in Score	p
Digit-Span Forward Test	T2	0.65 (±1.26)	0.25 (±0.49)	0.3698
	T3	0.93 (±1.09)	0.04 (±0.52)	**0.0044****
Digit-Span Backward Test	T2	0.21 (±0.53)	0.21 (±0.58)	0.8070
	T3	0.48 (±0.66)	0.27 (±0.67)	0.3242
Digit Symbol Test	T2	0.62 (±2.56)	0.13 (±2.43)	0.5157
	T3	0.58 (±2.19)	0.01 (±2.18)	0.4854
Trail Making Test A	T2	1.43 (±3.88)	0.17 (±3.00)	0.2040
	T3	1.26 (±3.14)	0.29 (±2.14)	0.2904
Trail Making Test B	T2	−0.29 (±3.13)	−1.05 (±3.90)	0.3262
	T3	0.85 (±2.56)	0.27 (±3.32)	0.4310
Verbal Fluency Test	T2	0.90 (±2.10)	0.26 (±1.07)	0.2278
	T3	1.32 (±1.82)	0.10 (±1.53)	**0.0331***
Word Recognition Test	T2	−0.19 (±0.63)	0.13 (±0.70)	0.5426
	T3	0.06 (±0.81)	−0.16 (±0.75)	0.2214

Note: The significance level was set at $p < 0.05$.
Values in boldface indicate p values less than 0.05.
*$p < 0.05$ of control group versus CCT group.
**$p < 0.01$ of control group versus CCT group.

the different experimental procedures. Given that CCT might encourage the participants to play with electronic devices, it is unknown whether they could benefit from the habit after the intervention. In respect of the characteristics of the participants, the control group also exhibit significant improvement in the Digit-Span Backward Test 12 weeks postintervention, which might indicate that the natural recovery process after the lung transplantation could be a confounding variable in the relation between retention time and CCT efficacy.

On a descriptive level, the participants in the CCT group showed improving, declining, or fluctuating performance in different tests in this research, so did the participants in the control group. These varied impacts of CCT on different cognitive domains were also observed in other experiments and meta-analysis (Hill et al., 2017; Kalbe et al., 2018; Lampit et al., 2014; Wu et al., 2018). Although there was little debate on the efficacy of CCT on global cognition, the effect of CCT on different cognitive domains varies according to the population types and the types of CCT programs administered (Hill et al., 2017; Kalbe et al., 2018; Kesler et al., 2013; Lampit et al., 2014; Wu et al., 2018). More than 18 conventional, unconventional, and customized CCT programs had been used on healthy cognitive, mild cognitive-impaired, demented, or community-dwelling subtypes in the elderly population (Hill et al., 2017; Ten Brinke et al., 2017). In an experiment involving healthy cognitive elderly people using two different CCT programs, one group showed significant improvement in figural memory and cognitive flexibility, while the other group showed additional significance in verbal memory and visuospatial skills (Kalbe et al., 2018). A meta-analysis revealed that CCT was efficacious on the improvement of attention, memory, and working memory in the mild cognitive-impaired elderly population, but these effects were negligible in the dementia cohort (Hill et al., 2017). Hence, results in this study agreed with the previous evidence that CCT is beneficial for the cognitive functioning in the elderly population, but it is also reasonable to observe varied impacts of CCT on different cognitive domains and the inconsistency with previous research.

There are a few limitations in this study. First, the small sample size limited the statistical power to detect the interaction between the variables, and further investigation should involve larger samples to draw a clearer conclusion. Second, this study was not double-blind, and the participants were aware of whether they were in the experimental or passive control group. This awareness might influence their attitude toward the intervention and subsequently affect the outcomes of the experiment. According to Kalbe et al. (2018), motivation and self-efficacy are positive predictors of cognitive training success, and this interaction between metacognitive attitude and training success is more evident in verbal and figural memory. Hence, the experimental group might have higher expectation for their performance during the tests, and it is difficult to differentiate the impact of the placebo effect from CCT. Although some studies suggested that there was no difference between the negative control and placebo group regarding the changes of cognitive function (Hill et al., 2017; Kulason et al., 2018), further investigation is still needed to determine the necessity of an active control or placebo group. Finally, in this study, healthy cognitive participants after lung transplantation and participants with POCD were not separately analyzed regarding the effect of CCT. Controversial conclusion has been drawn from different studies on whether CCT is more efficacious on healthy cognitive aging or cognitive-impaired population (Hill et al., 2017; Kalbe et al., 2018), which makes it hard to determine whether the changes in this study were more contributed by the POCD participants, cognitive participants, or both. Considering that POCD is a risk factor for medical nonadherence and mortality, POCD patients after lung transplantation could be more focused on to identify the most suitable CCT dosage and maintenance strategy for this cohort.

Further investigations can also be made on the customization of CCT for elderly lung recipients, as well as the transferability between the test scores, quality of life, and posttransplant survival rate. Despite the finding that CCT increased the scores in two of seven tests for the elderly lung recipients, it was not studied whether this CCT program is the most optimal for this population. It was suggested in a meta-analysis that nontraditional CCT approaches such as virtual reality and Nintendo are more stimulating and result in greater effect (Hill et al., 2017). It was also suggested that a CCT program focusing on certain cognitive domain could improve the function in this domain better than the other ones (Kulason et al., 2018). Therefore, there is a great scope of comparison that can be made between the differently structured CCT and current CCT, which can be tailored to benefit the elderly lung-transplant recipients. Moreover, although it has been demonstrated that neurocognitive impairment is negatively associated with quality of life and posttransplant survival (Smith et al., 2014), it was not clear whether this association is a causal relation or due to other confounding variables. Further research should be designed to determine whether the improved performance in the neurocognitive assessment is associated with a better quality of life and a higher survival rate.

CONCLUSIONS

In conclusion, this study provides information about the feasibility and efficacy of home-based CCT on the cognitive functioning in the elderly population after lung transplantation. It could be a feasible strategy as more than 90% participants adhered to the training protocol. It could not be claimed that CCT improves the cognitive performance better than the usual care in this population in all cognitive domains, but it did exhibit significant advantage in improving the verbal memory over the usual care. There are insufficient data suggesting whether these effects are attributed to POCD or normal cognitive participants; thus, studies with modified regimens are required to determine the efficacy of CCT on the treatment of POCD. Furthermore, longer-term and more comprehensive research is necessary to investigate the different types of CCT and the association between CCT intervention and posttransplant survival.

DISCLOSURE

The authors declare no conflict of interest.

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"Formal Thought Disorder" in a General-Community Sample With Elevated Schizotypal Traits: Erratum

In the May 2019 issue of *The Journal of Nervous and Mental Disease* in the article by Deyo and Langdon, "'Formal Thought Disorder' in a General-Community Sample With Elevated Schizotypal Traits", the opening sentence should read as follows, "Disturbances of speech are characteristic of schizophrenia, and are traditionally referred to as formal thought disorder (FTD)."

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Deyo C, Langdon R (2019) "Formal Thought Disorder" in a General-Community Sample With Elevated Schizotypal Traits. *J Nerv Ment Dis*. 207:410–416.