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CHAPTER

6

Can exercise improve activities of daily living in patients with dementia? A nine-week randomized, controlled trial.¹

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ABSTRACT

Objectives

To determine 1) the effects of a nine-week-long combined aerobic and strength exercise program, and an aerobic-only exercise program on proxy-reported and performance-based activities of daily living (ADL), and 2) the mediating effect of exercise induced changes in motor and cognitive function on changes in ADL in patients with dementia.

Methods

Patients with dementia (N = 105, age = 85.6 ± 5.1 years) participated in a nine-week, parallel, three-group, single-blind, randomized, controlled trial.

Intervention

Each 9-week-long intervention consisted of 36, 30-minute-long sessions. A Combined group (N = 35) received and completed two strength and two walking sessions per week. An Aerobic group (N = 35) completed four walking sessions, and a Social group (N = 35) four social visits per week.

Results

There was a group effect for pre-posttest difference scores in proxy-report KATZ ($\chi^2 = 8.1(2)$, $p = .018$), and performance-based Erlangen-ADL ($\chi^2 = 16.4(2)$, $p < .001$) and 7-item Physical Performance Test (PPT-7) ($\chi^2 = 11.9(2)$, $p = .003$). Compared to the Social group, the Combined group significantly improved on KATZ ($Z = -2.8$, $p = .010$), Erlangen-ADL ($Z = -3.8$, $p < .001$), and PPT-7 ($Z = -3.3$, $p = .002$), whereas the Aerobic group only improved on the Erlangen-ADL ($Z = -2.9$, $p = .008$). In the Combined group, pretest-posttest difference scores on global cognition significantly mediated KATZ, while leg-muscle strength mediated Erlangen-ADL, and leg-muscle strength and walking endurance mediated PPT-7.

Conclusion

Both motor (i.e., walking endurance and leg strength) and cognitive (i.e., global cognition) function mediate the superior effects of a combined aerobic and strength training versus an aerobic-only training in improving ADL in patients with dementia.

INTRODUCTION

Dementia is associated with cognitive and motor impairments, which in turn leads to lower levels in activities of daily living (ADL).^{1,3} In addition to motor and cognitive decline, impaired cognitive coping strategies, that could compensate for physical limitations, exacerbate ADL disability in patients with dementia. ADL disability leads to increased dependence in daily life, which contributes to lower quality of life⁴ and greater caregiver effort, care burden, and long-term care costs.^{5,6} To combat these emerging personal and socio-economic problems it is of high clinical relevance to develop interventions that slow the evolution of ADL disability in patients with dementia.

Specific risk factors, including physical inactivity, can accelerate the progression of ADL disability.⁷ Nursing home residents with dementia have an increased risk for becoming inactive because these patients often have thoughts that make them reluctant from becoming physically active, and they also have great difficulties in initiating movement.⁸ In addition, institutionalized patients with dementia often live in a closed off ward that limits free movement within the facility. Patients who are physically inactive are at major risk for a decline in motor and cognitive function.^{9,10} Therefore, decreasing physical inactivity through an exercise program could slow the decline in both physical and cognitive function in patients with dementia and as a result, slow ADL disability.¹¹

The hypothesis that exercise is beneficial for ADL in patients with dementia has been examined only to a limited extent.¹¹ To date, five studies¹²⁻¹⁶, of which three with limited sample size ($N < 8$ $N \leq 24$)¹³⁻¹⁵ and one without a control group¹⁶, showed inconsistent results with small to large ADL effects after a specific aerobic or strength exercise program. In healthy old people¹⁷ and in older patients with dementia¹⁸, a combination training consisting of aerobic and strength exercise yielded the strongest cognitive and motor effects. Therefore, we hypothesize that a combined aerobic and strength exercise program is more effective in improving ADL than a single-component exercise program.

The previous ADL studies only used proxy-reported ADL measures, which are, compared to performance-based ADL tests, less valid (e.g., prone to subjective influence and social desirability bias) and less sensitive to detect changes.¹⁹ The use of proxy-report measures can overestimate (e.g., social desirability bias) or underestimate (e.g., limited sensitivity to change) intervention effects.²⁰ Clinical trials should therefore include both proxy- and performance-based ADL measures with appropriate sample sizes to study the effects of exercise on care related proxy-ADL perception and the patient-based ADL performance. We assessed both ADL

measures to study the effect of exercise on ADL.

To date, there are no data on how exercise-induced adaptations in motor and cognitive function mediate improvements in ADL in patients with dementia. Based on several disability models^{3, 21-23}, we expect that by reducing motor impairments (e.g., improve walking endurance, strength, balance, mobility) via physical exercise, motor performance-based ADL will improve (e.g., transfers in the living room, picking up an object from the floor, lifting a heavy object). Regular physical exercise may also improve cognitive functions (e.g., global cognition, memory, and executive function)^{24, 25}, which are involved in cognitively challenging ADL tasks (e.g., reasoning and planning). Therefore, we hypothesized that improvements in motor and cognitive function after physical exercise positively mediate improvements in ADL.

In sum, the primary aim of the study was to determine the effects of a nine-week-long combined aerobic and strength exercise program, compared to an aerobic-only exercise program, on proxy-reported and performance-based ADL in patients with dementia. The secondary objective was to study the mediating effect of exercise induced changes in motor and cognitive function on changes in ADL.

METHODS

Ethics statement

The Medical Ethics Committee of the University Medical Center Groningen, The Netherlands, approved the research protocol according to the principles expressed by the Declaration of Helsinki, and gave permission for the procedures of this study. Prior to entering the study, we obtained written consent from each patient's legal representative.

Design and procedures

The present study is part of a large randomized clinical trial in patients with dementia, in which the effects of a combination of aerobic and strength sessions, compared to aerobic only or social sessions, on cognitive and motor function are studied.¹⁸

In the present study, we compared the effects of two exercise interventions with a control group on ADL function in patients with dementia. The study design was a nine-week-long, parallel, three-group, single-blind, randomized, controlled trial. Parallel to the combined aerobic and strength exercise group (Combined group), an aerobic-only group (Aerobic group), and a social visit group (Social group) were allocated. Baseline measurements (baseline, T0) were done before randomization procedures, and retests were done after the nine-week-long intervention (time 9-weeks, T1).

Between January 2011 and May 2013, patients were recruited from seven specialized nursing homes in Northern Netherlands. First, a geriatrician checked the following initial eligibility criteria: age 70 or older, diagnosis of dementia, and absence of serious health problems. Next, a trained Human Movement Sciences (HMS) research-assistant tested the patients for the following additional inclusion criteria: Mini Mental State Examination score (MMSE) ≥ 9 and ≤ 23 , and able to perform the timed up & go test.²⁶ For those who passed these five criteria, baseline performance-based ADL, cognitive, and motor function were assessed by a trained HMS research-assistant. A nurse, who worked closely with a patient, completed the proxy-reported ADL (i.e., KATZ-index). The test administrators were then blinded to patients' group assignment. After baseline measurements, participants were randomly assigned to one of three groups, by using numbered containers, stratified according to nursing home, gender, and MMSE score (allocation ratio 1:1:1). A scientist unrelated to the study performed the procedure.

Intervention

We have recently described in detail the three intervention programs.^{18, 27} Briefly, 18 trained HMS researchers administered 30-minute-long, one-on-one guided sessions in each intervention program. The Combined group participated in two strength and two walking sessions each week, for a total of nine weeks. Aerobic and strength

training sessions were alternated. This exercise program improved motor (i.e., walking endurance, leg strength, and balance) and cognitive function (i.e., global cognition, executive function, memory).¹⁸ The Aerobic group participated in four walking sessions each week, and the Social group participated in four social visits each week, for nine weeks total.

Strength exercise

Strength exercises for the Combined group focused on lower-limb strengthening. The exercises were as follows: (1) seated knee extension, (2) plantar flexion through toe raises while holding both hands of the trainer, (3) hip abduction by moving the straight leg sideways while standing behind and holding on to a chair, and (4) hip extension by moving the straight leg backwards while standing behind and holding on to a chair.

Aerobic exercise

Aerobic exercise consisted of moderate to high intensity walking sessions that were performed in the corridors of the nursing home, or on paved outdoor walking paths near the nursing home. If a participant requested rest, an appropriate rest period was included in the 30-minute-long session. As soon as patients recovered, walking was resumed. The training intensity was adjusted by varying the distances per session.

Social intervention

The Social group received 30-minute-long, one-on-one social visits. During social visits participants talked with the HMS research-assistant, while sitting in a chair.

Measurements

At T0 and T1, a nurse who worked closely with a participant filled in a proxy-reported KATZ questionnaire. Furthermore, the performance based Erlangen-ADL test (E-ADL), 7-item physical performance test (PPT-7), a motor function test battery, and a cognitive function test battery were assessed by a trained HMS research-assistant who was blinded for the treatment conditions.

KATZ questionnaire

The KATZ is a proxy-reported questionnaire. The test assesses dependency in basic functional, care-related ADL.²⁸ The KATZ consists of six items (bathing, dressing, toileting, transferring, continence, and feeding), which were scored on a 3-point Likert scale. A higher score on the KATZ indicated that more help was needed during ADL activities, which was provided by the nurse. Per item, a score 1 represented complete independency, a score 2 moderate dependency, and a score 3 complete dependency. The sum score of six items was used as outcome variable. A score of 6 indicated complete ADL independency, 12 moderate ADL dependency, and 18

indicated maximal dependency on ADL. For interpretation purposes in the analysis, the KATZ difference scores were multiplied by -1, thereby indicating that a positive difference score represented an improvement on the KATZ. The KATZ is a frequently used functional ADL measure in residential care settings, and is reliable to measure patients' functional status.²⁹

Erlangen Test of Activities of Daily living (E-ADL)³⁰

The E-ADL is a performance based instrumental-ADL test that consists of six items: pouring a drink, spreading butter on a sandwich and cutting the sandwich, open a little cupboard with a key, wash and dry hands, and tie a bow on a small wrapped present. Points were given for each correctly performed step within each of the six items. E-ADL scores ranged from 0 to 31 with a higher score indicating better ADL. The E-ADL was specifically developed for patients with dementia and showed good validity and test-retest reliability.³¹

Physical Performance Test adjusted 7-items³²

The PPT-7 is a performance based motor function ADL test.³² The PPT-7 consists of seven items: writing a sentence, transfer five beans from a bowl into a cup with a teaspoon, lifting a book onto a shelf, put on a coat, pick up a coin from the floor, walk 50 feet (15.24 meters), and turning 360 degrees while standing in one place. Each item was scored on a 4-point Likert scale according to preset time limits, and the patients' ability to perform the test according to protocol. The total score was the sum of seven items and scores ranged from 0 - 28, with higher scores indicating better motor ADL performance. The PPT-7 was found feasible and reliable in patients with dementia.³³

Cognitive and motor tests

Details of the cognitive and motor tests are described in a study by Bossers et al. (2014).²⁷

Thirteen cognitive tests were assessed, which covered the following cognitive domains: global cognition (Mini Mental State Examination), visual memory (visual memory span forward test, faces recognition test, pictures recognition test), verbal memory (eight-words test direct recall, eight-words test recognition, digit span forward test), and executive function (visual memory span backward test, digit span backward test, stroop test, verbal fluency test, picture completion test, trail making test-A).

Eight motor tests were assessed for walking endurance (six minutes walking test), leg strength (30-seconds sit-to-stand test, maximal knee extension strength with a dynamometer), mobility (6-meter walk test, timed up & go), and balance (frailty and injuries cooperative studies of intervention techniques - subtest 4 (FICSIT-4), figure

of eight test, Groningen Meander Balance Test).

Statistical analysis

SPSS 20.0 was used for data analysis, and two-sided alpha was set at 0.05. Baseline differences of group characteristics between the three groups were analyzed with Chi-squared tests and ANOVA tests.

KATZ, E-ADL, and PPT-7 data were not normally distributed, and homogeneity of variances between groups was not supported. Therefore, Kruskal-Wallis tests between the difference scores of the KATZ, E-ADL, and PPT-7 were done to compare the three groups with respect to the effects on ADL. In addition, post-hoc pairwise comparisons were done using Mann-Whitney tests with Bonferroni corrections to correct for alpha inflation (i.e., two comparisons; Combined vs. Social and Aerobic vs. Social). The magnitude of effects between the Combined and Social group, and Aerobic and Social group were displayed as Cohen's *d* effect sizes.³⁴ Cohen's benchmarks were used to indicate small ($d = 0.20$), moderate ($d = 0.50$), and large ($d = 0.80$) effect sizes.

To explore mediating effects of pre-posttest change in cognitive and motor domain test scores on pre-posttest change in ADL performance, a mediation analysis was done following Hayes & Preacher (2013).³⁵ Multiple regression analyses were conducted to assess the three proposed mediation models for KATZ, E-ADL, and PPT-7 difference scores (Figure 6.2). Dummy coding was used to test the direct and indirect effect of the Combined and Aerobic group, using the Social group as reference group on each of the three dependent ADL variables. Cognitive and motor domain difference scores, published previously¹⁸, were used as mediators. Bootstrap with 5000 resamples was used for the regression analysis and the 95% confidence interval calculation.³⁵

RESULTS

Table 6.1. Baseline characteristics of the Combined group (N = 35), Aerobic group (N = 35) and Social group (N = 35) as mean (SD) or percentage per group.

Characteristic	Combined group	Aerobic group	Social group	p-value assessing group difference
Age, years	85.7 (5.2)	85.5 (5.4)	85.7 (4.8)	.976 ^a
Male (%)	22.9%	22.9%	31.4%	.368 ^b
Dutch education level (%)				.911 ^b
Finished primary school or lower	17.2%	22.9%	11.5%	
Lower than finished higher education	60.0%	48.6%	57.2%	
Finished higher education	22.8%	28.5%	31.3%	
Use of walking aid (%)	40.0%	65.7%	60%	.076 ^b
Mini Mental State Examination score ^c	15.9 (4.4)	15.3 (4.8)	15.9 (4.3)	.821 ^a
Functional Comorbidity Index ^d	2.8 (1.3)	3.2 (1.8)	3.4 (1.7)	.261 ^a
Cause of dementia (%)				.374 ^b
Alzheimer's Disease	57.1%	60.0%	45.7%	
Vascular Dementia	14.3%	20.0%	14.3%	
Alzh. Disease / Vasc. Dementia	11.4%	17.1%	20.0%	
Type not reported	17.2%	2.9%	20.0%	

Note: ^a, ANOVA; ^b, Chi-Square Test; ^c, theoretical range 0 – 30 and a higher score indicates better performance; ^d, theoretical range 0 – 18 and a higher score indicates more comorbidities.

Changes in total ADL outcome scores

Figure 6.1 describes the study flow. In total, 495 institutionalized patients were screened for eligibility of whom 118 enrolled in the study. Table 6.1 shows that there were no significant differences for population characteristics at baseline between the three groups. No significant differences were found in adherence rate between the Combined (89.1% ± 10.2%), Aerobic (90.1% ± 9.1%), and Social group (92.8% ± 6.7%) ($p = .136$).

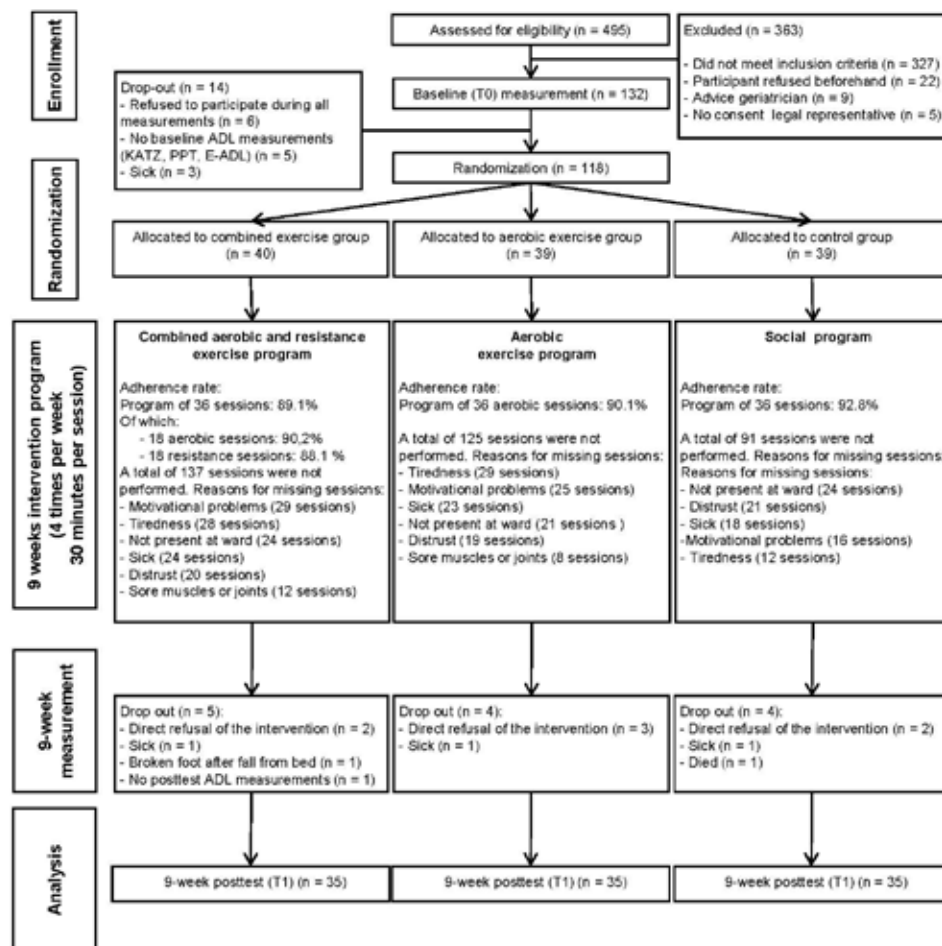


Figure 6.1. CONSORT flowchart of participants

Table 6.2 presents the ADL-data for the KATZ, E-ADL, and PPT-7. The three groups did not significantly differ at baseline for the three ADL tests. Kruskal-Wallis tests revealed a group effect for pre-posttest difference scores in KATZ ($\chi^2 = 8.09(2)$, $p = .018$), E-ADL ($\chi^2 = 16.40(2)$, $p < .001$), and PPT-7 ($\chi^2 = 11.93(2)$, $p = .003$).

For the KATZ, Mann-Whitney tests showed that pretest-posttest difference scores in the Combined group, compared to the Social group, were significantly larger ($Z = -2.787$, $p = .010$) with a small effect size ($d = 0.32$). Changes between the Aerobic and the Social group were similar ($Z = -0.987$, $p = .646$).

For the E-ADL, Mann-Whitney tests showed that pretest-posttest difference scores in the Combined group, compared to the Social group, were significantly higher ($Z = -3.833$, $p < .001$) with a large effect size ($d = 0.85$). Pretest-posttest difference scores between the Aerobic group and Social group was also significantly higher ($Z = -2.916$, $p = .008$) with a moderate effect size ($d = 0.53$).

For the PPT-7, Mann-Whitney tests showed that pretest-posttest difference scores in the Combined group, compared to the Social group, was significantly higher ($Z = -3.337$, $p = .002$) with a moderate effect size ($d = 0.62$). Changes between the Aerobic and the Social group were similar ($Z = -1.664$, $p = .192$).

Mediating effect of cognitive and motor difference scores on ADL difference scores

Figure 6.2 illustrates the three mediation models, which represent the effects of the Combined versus Social (Figure sub-part a), and Aerobic versus Social group (Figure sub-part b) on pretest-posttest difference scores of the KATZ (Figure 6.2, panel I), E-ADL (Figure 6.2, panel II), and PPT-7 (Figure 6.2, panel III). For clarity reasons, sub-panels a and b are presented separately but represent data from one model. Significant mediating paths are drawn with bold lines.

KATZ

Only the difference score in global cognition significantly mediated the effect between the Combined group and KATZ difference score. As Figure 6.2-Ia illustrates, the standardized mediating effect of the Combined group on KATZ via global cognition was $(.81) \times (.22) = .18$ ($CI = .05$ to $.41$). Thus, the mediation was statistically significant. There were no statistically significant mediating effects in the Aerobic group.

E-ADL

The difference score in leg strength significantly mediated the effect between the Combined group and E-ADL difference score. As Figure 6.2-IIa illustrates, the standardized mediating effect of the Combined group on E-ADL via leg strength was $(.72) \times (.26) = .19$ ($CI = .03$ to $.43$). Thus, the mediation was statistically significant. There were no statistically significant mediating effects in the Aerobic group.

PPT-7

The difference score in walking endurance and leg strength significantly mediated the effect between the Combined group and PPT-7 difference score. As Figure 6.2-IIIa illustrates, the standardized indirect effect of the Combined group on PPT-7 via walking endurance was $(.69) \times (.21) = .15$ ($CI = .01$ to $.36$) and via leg strength was $(.72) \times (.23) = .17$ ($CI = .01$ to $.43$). Thus, these indirect effects were statistically significant. There were no statistically significant mediating effects in the Aerobic group.

DISCUSSION

The primary aim of this clinical trial was to determine whether physical training improves ADL performance in patients with dementia, and whether combined aerobic and strength training is superior to aerobic-only training. The second aim was to explore whether improvements in cognition and motor function, elicited by the exercise programs, mediated the improvements in ADL performance.

Although both the Combined and Aerobic exercise programs improved ADL performance in patients with dementia, a key finding of the present study was that a combination of aerobic and strength training was superior in improving proxy-reported and performance-based ADL, when compared with aerobic-only training. We also observed smaller effect sizes for the changes in ADL measured by proxy-reporting (i.e., KATZ test), confirming previous findings of small effects in a similar patient population.^{12, 13} To the best of our knowledge, the present study is the first to compare intervention-produced changes in ADL by both proxy-based and performance-based measurements. We found that the changes measured by performance- versus proxy-based ADL tests had 1.9-2.7 times larger effect sizes. Finally, the current mediation analysis is the first to suggest that factors that mediate improved ADL in patients with dementia include improved walking endurance, leg strength, and global cognition.

Due to the rapid decline in ADL in patients with dementia, a question of high clinical importance is whether a short-term exercise program can slow the deterioration in ADL. The current small effect size in proxy-reported KATZ after the nine-week-long exercise program, are in line with a one-year-long and twelve-week-long study in patients with dementia.^{12, 13} However, the current program was respectively 43 and 3 weeks shorter, and we delivered the training program on a one-on-one basis. Furthermore, sessions were twice as short, and were administered twice as frequently. Because the current nine-week-long and the previous twelve-week-long exercise program¹³ had similar adherence rates, a shorter training period may have resulted in the 55.6% higher adherence rate, compared with the one-year-long group intervention.¹² These data imply that an exercise program with relatively short duration, but high session frequency, can be as effective in terms of proxy-reported ADL as a long duration but lower session frequency program. However, it remains unclear whether these effects are caused by a difference in exercise program setting or by a difference in adherence to the program. Further, the previous one-year-long study could also have resulted in similar adherence rates over a nine-week-long period, as seen in the current work, but the data cannot be extracted from the study to support this idea.¹²

We found large differences in effect sizes between the two measures: zero to small effects, when using the proxy-reported ADL measures, compared with moderate to large effects, when using the performance-based ADL measures. Proxy-report measures are known to cause either an overestimation (due to social desirability bias) or an underestimation of the actual effect (due to limited sensitivity for change).²⁰ Our data confirm the underestimation of ADL performance when measured with a proxy-reported ADL test. Specifically, we think that this inaccuracy is related to a lack of sensitivity to change in the KATZ questionnaire, that minimized the variability in the training effects. Most likely, the narrowness of the 3-point Likert scale is causing the poor sensitivity of this test. Therefore, there is a need in future studies to use proxy-report ADL-questionnaires with a wider scoring range, making the questionnaire more sensitive to change in ADL performance.

In line with the current study, previous studies found beneficial effects on proxy-reported ADL performance after exercise training.^{12, 13, 15} However, these studies failed to determine how reduced impairments convert to improved ADL. The current mediation analysis is the first to suggest that exercise intervention-induced improvements in global cognition significantly mediate the increases in proxy-reported ADL performance. Such a mediation between proxy-reported ADL and global cognition may be explained by the fact that proxy-questionnaires also involve the experience of the nurse in handling more complex ADL tasks, which require planning and help from a nurse. By improving global cognition, patients with dementia may be better able to perform basic ADL tasks that include orientation in time and space, understanding of instructions, and remembering and recognizing tasks. Therewith, communication and cooperation between nurse and patient may be enhanced, resulting in better ADL performance and lower care burden.³⁶ On the other hand, motor related improvements in leg-muscle strength and walking endurance mediate improvements in performance-based ADL. The performance-based measures include single-component ADL tasks that require little planning, and are administered in a fixed pre-set environment. For these performance-based ADL tasks, improved motor function may be more important than cognitive function. Motor functions are proposed to be an even stronger factor in healthcare burden than cognitive function.³⁶ Based on the present results, we recommend that future exercise intervention studies should combine aerobic and strength training to most effectively increase cognitive and motor function because such changes can in turn improve proxy-based and performance-based ADLs in patients with dementia, thereby lowering healthcare burden.

The current study has some limitations. First, it was not possible to blind the nurses who filled in the KATZ to the treatment because they worked with the participant on a daily basis. However, based on the underestimation of the proxy-reported ADL effect, it seems that there was no or little desirability bias in the current study.

Furthermore, as a consequence of a general research setting in the clinic, an involved nurse, who fills in a proxy-report, is aware of patients' daily routines and activities. Therefore, one advantage of using a performance-based ADL test, in addition to proxy test, is that such a test informs the nurse what a patient with dementia can still do, compared with proxy-report information that provides information on what the nurse thinks a patient can do. Information derived from a combination of proxy- and performance-based ADL data is of clinical interest because it can tune nurses' perception as to what patients can and should be able to do in terms of ADL. This combined information can be used to increase ADL independency and therewith, improve quality of life in patients with dementia.⁴

CONCLUSION

In patients with dementia, a short-term, nine-week-long combined aerobic and strength exercise program is superior in improving ADL, compared with aerobic-only exercise. Factors that mediate improved ADL in patients with dementia include improved walking endurance, leg strength, and global cognition. The current study stresses the importance of physical exercise participation, as part of a physically active lifestyle, in the maintenance of ADL in institutionalized elderly with dementia.

REFERENCES

1. Feldman HH, Van Baelen B, Kavanagh SM, Torfs KE. Cognition, function, and caregiving time patterns in patients with mild-to-moderate Alzheimer disease: A 12-month analysis. *Alzheimer Dis Assoc Disord*. 2005;19:29-36.
2. Sauvaget C, Yamada M, Fujiwara S, Sasaki H, Mimori Y. Dementia as a predictor of functional disability: A four-year follow-up study. *Gerontology*. 2002;48:226-233.
3. Barberger-Gateau P, Fabrigoule C, Amieva H, Helmer C, Dartigues JF. The disablement process: A conceptual framework for dementia-associated disability. *Dement Geriatr Cogn Disord*. 2002;13:60-66.
4. Andersen CK, Witttrup-Jensen KU, Lolk A, Andersen K, Kragh-Sorensen P. Ability to perform activities of daily living is the main factor affecting quality of life in patients with dementia. *Health Qual Life Outcomes*. 2004;2:52.
5. Boersma F, Van Den Brink W, Deeg DJ, Eefsting JA, Van Tilburg W. Survival in a population-based cohort of dementia patients: Predictors and causes of mortality. *Int J Geriatr Psychiatry*. 1999;14:748-753.
6. World Health Organization. *Dementia: A Public Health Priority*. Geneva, Switzerland: WHO Press, World Health Organization; 2012.
7. Sakurai T, Iimuro S, Sakamaki K, et al. Risk factors for a 6-year decline in physical disability and functional limitations among elderly people with type 2 diabetes in the Japanese elderly diabetes intervention trial. *Geriatr Gerontol Int*. 2012;12 Suppl 1:117-126.
8. Perri R, Monaco M, Fadda L, Caltagirone C, Carlesimo GA. Neuropsychological correlates of behavioral symptoms in Alzheimer's disease, frontal variant of frontotemporal, subcortical vascular, and lewy body dementias: A comparative study. *J Alzheimers Dis*. 2013; 39:669-677.
9. Nyberg L, Gustafson Y, Janson A, Sandman PO, Eriksson S. Incidence of falls in three different types of geriatric care. A Swedish prospective study. *Scand J Soc Med*. 1997;25:8-13.
10. Lovden M, Xu W, Wang HX. Lifestyle change and the prevention of cognitive decline and dementia: What is the evidence? *Curr Opin Psychiatry*. 2013;26:239-243.
11. Blankevoort CG, van Heuvelen MJ, Boersma F, Luning H, de Jong J, Scherder EJ. Review of effects of physical activity on strength, balance, mobility and ADL performance in elderly subjects with dementia. *Dement Geriatr Cogn Disord*. 2010;30:392-402.
12. Rolland Y, Pillard F, Klapouszczak A, et al. Exercise program for nursing home residents with Alzheimer's disease: A 1-year randomized, controlled trial. *J Am Geriatr Soc*. 2007;55:158-165.
13. Santana-Sosa E, Barriopedro MI, Lopez-Mojares LM, Perez M, Lucia A. Exercise training is beneficial for Alzheimer's patients. *Int J Sports Med*. 2008;29:845-850.
14. Kwak YS, Um SY, Son TG, Kim DJ. Effect of regular exercise on senile dementia patients. *Int J Sports Med*. 2008;29(0172-4622; 0172-4622; 6):471-474.
15. Venturelli M, Scarsini R, Schena F. Six-month walking program changes cognitive and ADL performance in patients with alzheimer. *Am J Alzheimers Dis Other Demen*. 2011; 26:381-8.
16. Aman E, Thomas DR. Supervised exercise to reduce agitation in severely cognitively impaired persons. *J Am Med Dir Assoc*. 2009;10:271-276.
17. Colcombe S, Kramer AF. Fitness effects on the cognitive function of older adults: A meta-analytic study. *Psychol Sci*. 2003;14:125-130.
18. Bossers WJ, van der Woude LH, Boersma F, Hortobagyi T, Scherder EJ, van Heuvelen MJ. A nine-week-long aerobic and strength training program improves cognitive and motor function in patients with dementia: A randomized, controlled trial. *Am J Geriatr Psychiatry*. 2014 (under revision).
19. Puente AN, Terry DP, Faraco CC, Brown CL, Miller LS. Functional impairment in mild cognitive impairment evidenced using performance-based measurement. *J Geriatr Psychiatry Neurol*. 2014. Epub ahead of print PMID: 24763070.
20. Fisher RJ. Social desirability bias and the validity of indirect questioning. *Journal of consumer research*. 1993;20:303-315.
21. NAGI SZ. A study in the evaluation of disability and rehabilitation potential: Concepts, methods, and procedures. *Am J Public Health Nations Health*. 1964;54:1568-1579.
22. Verbrugge LM, Jette AM. The disablement process. *Soc Sci Med*. 1994;38:1-14.
23. Jette AM. Toward a common language for function, disability, and health. *Phys Ther*. 2006;86:726-734.
24. Behrman S, Ebmeier KP. Can exercise prevent cognitive decline? *Practitioner*. 2014;258:17-21, 2-3.
25. Forbes D, Thiessen EJ, Blake CM, Forbes SC, Forbes S. Exercise programs for people with dementia. *Cochrane Database Syst Rev*. 2013;12:CD006489.
26. Podsiadlo D, Richardson S. The timed "up & go": A test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc*. 1991;39:142-148.

27. Bossers WJ, Scherder EJ, Boersma F, Hortobagyi T, van der Woude LH, van Heuvelen MJ. Feasibility of a combined aerobic and strength training program and its effects on cognitive and physical function in institutionalized dementia patients. A pilot study. *PLoS One*. 2014;9:e97577.
28. Katz S, Downs TD, Cash HR, Grotz RC. Progress in development of the index of ADL. *Gerontologist*. 1970;10:20-30.
29. Ciesla JR, Shi L, Stoskopf CH, Samuels ME. Reliability of katz's activities of daily living scale when used in telephone interviews. *Eval Health Prof*. 1993;16:190-203.
30. Luttenberger K, Schmiedeberg A, Grassel E. Activities of daily living in dementia: Revalidation of the E-ADL test and suggestions for further development. *BMC Psychiatry*. 2012;12:208-244X-12-208.
31. Graessel E, Viegas R, Stemmer R, Kuchly B, Kornhuber J, Donath C. The Erlangen test of activities of daily living: First results on reliability and validity of a short performance test to measure fundamental activities of daily living in dementia patients. *Int Psychogeriatr*. 2009;21:103-112.
32. Reuben DB, Siu AL. An objective measure of physical function of elderly outpatients. the physical performance test. *J Am Geriatr Soc*. 1990;38:1105-1112.
33. Farrell MK, Rutt RA, Lusardi MM, Williams AK. Reliability of the physical performance test in people with dementia. *Phys Occup Ther Geriatr*. 2010;28:144-153.
34. Cohen J. Statistical power analysis for the behavioural sciences (2nd ed.). In: Hillsdale New Jersey: Lawrence Erlbaum. 1988.
35. Hayes AF, Preacher KJ. Statistical mediation analysis with a multicategorical independent variable. *Br J Math Stat Psychol*. 2013. Epub ahead of print doi: 10.1111/bmsp.12028.
36. Kang HS, Myung W, Na DL, et al. Factors associated with caregiver burden in patients with alzheimer's disease. *Psychiatry Investig*. 2014;11:152-159.

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