A randomised controlled trial on the effect of exercise on physical, cognitive and affective function in dementia subjects

ORIGINAL ARTICLE

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ABSTRACT

Objectives. To study the effect of an exercise intervention on physical function, cognition and affect in demented elderly subjects.

Methods. A randomised controlled trial of 85 dementia patients attending the memory clinic of a regional hospital in Hong Kong was conducted between October 2005 and August 2007 inclusive. The intervention group received aerobic exercise training with treadmill, bicycle, arm ergometry and flexibility exercises carried out for 1 hour twice a week for 12 weeks. The control group received conventional medical treatment. Physical performance was evaluated using 6-minute walking distance, functional reach, the Berg Balance Scale and the SF-12 quality-of-life questionnaire. Cognitive function was measured by the Mini-Mental State Examination and Alzheimer Disease Assessment Scale-Cognitive Subscale. The Cornell Scale for Depression in Dementia was used to test for presence of depressive symptoms and carer stress was measured by the Zarit Burden Interview. For each outcome measure, the mean change from baseline was calculated at 3 monthly intervals, for up to 12 month.

Results. Improved physical performance was significantly greater in the exercise group than in the routine medical care group. A significant difference between groups in favour of the exercise programme was observed for the 6-minute walking distance (12-month mean treatment difference 29.75, p=0.014) and functional reach (12-month mean treatment difference 2.63, p=0.009). There was no statistically significant difference between the 2 groups with respect to cognitive function. Exercise intervention did not have any effect on depression.

Conclusion. A simple exercise programme led to a significant improvement in physical function but did not have any effect on mental function.

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INTRODUCTION

The prevalence of dementia increases with age. In Hong Kong it was present in 4% of patients aged 65 years or older, increasing to 6% in those aged 70 years or more.[1] It presents a major health problem that impacts people's ability to maintain occupational and social function.[2]

Exercise has multiple positive effects in older adults, including those with disability.[3] Exercise also prevents and reduces the risks of developing secondary conditions that arise from functional decline and physical disease.[4,5] Exercise has been found to benefit elderly people with cognitive impairment. A meta-analytic review of 30 studies reported that exercise training improves physical fitness, physical function, cognitive function and positive behaviour in people with dementia.[6] Physical activity may be protective for Alzheimer's disease due to better-maintained cerebral perfusion and cerebrovascular health.[7] Aerobic fitness training appears to have an association with reduced brain tissue loss in ageing humans.[8]

Few older adults exercise regularly. Reasons for non-participation in exercise are inconvenience, lack of time, orthopaedic and other health problems and belief that they get enough exercise elsewhere.[9]

Persons with cognitive decline often need long-term care that leads to institutionalisation. Nursing homes generally lack environmental stimulation and physical activity opportunities. Therefore it is recommended that regular physical exercise should be encouraged in both healthy and cognitively impaired elderly people.

Aim

Few epidemiological studies have examined the role of physical activity on the risk of cognitive impairment and dementia in older persons. Exercise may be protective for dementia. Alzheimer's disease in particular has been the subject of a case-control study, using prevalent cases,[10] but findings have not been consistently replicated.[11] Discordant results have also been reported in a few prospective studies.[12] There was also lack of clinical evidence on the effect of exercise in Chinese demented patients. The aim of this study was to prospectively investigate the effect of aerobic exercise on physical function, cognition, and affect of demented patients and further explore the stress associated with caring for these patients.

MATERIALS AND METHODS

A 12-month randomised controlled study of dementia patients was carried out in the memory clinic of a regional hospital in Hong Kong. Consecutive patients with a diagnosis of dementia according to the DSM-IV-TR criteria (American Psychiatric Association 2000) were randomised into one of two groups, the exercise group or the conventional treatment group. Subjects on drug treatment for dementia were also included.

Inclusion criteria for the patients were: mild-to-moderate dementia, Cantonese version Mini-Mental State Examination (MMSE) scores of 10 to 26, age >60, being community dwelling, ambulatory, and having a caregiver that was willing to participate and escort the patient to hospital for training and assessment. Patients with severe dementia (MMSE<10) were excluded.

Enrolment began in November 2005 and follow-up ended in August 2007. The Hospital Authority Cluster Ethical Committee approved this study. For each subject, baseline demographic data, as well as concomitant medical problems, types and number of medications taken and duration of dementia were collected.

Intervention

Aerobic exercise training included: treadmill, bicycle and arm ergometry (carried out in our geriatric day hospital), and ten-minute flexibility training (performed at the start of each session). Patients attended training sessions twice per week. Each session lasted 45 to 60 minutes and the total duration of treatment was 3 months. A physiotherapist supervised each participant. Control groups were followed up for assessment at 3 monthly intervals.

Outcome variables

Physical function was measured by: the SF-12 quality-of-life questionnaire, 6-minute walk test, functional reach and Berg Balance Scale measure. The SF-12 assesses general health status and has been used extensively in older adults. Higher SF-12 scores indicate better health functioning.[13] Functional reach was measured by asking the subject to stand next to a wall holding their arm parallel to a meter stick attached to the wall at shoulder height. Subjects were instructed to reach forward as far as possible without losing balance. The Berg Balance Scale was used to measure balancing ability of the subjects; a high score means better balancing ability. Cognitive function was measured by the MMSE and the Alzheimer's Disease Assessment Scale-Cognitive subscale (ADAS-Cog).[14] Affect was measured by the Cornell

Scale for Depression in Dementia (Chinese version). It is a 19-item scale that measures depression after interviews with the patient and caregiver. Items are 'mood and related signs', 'behaviour disturbances', 'cyclical function and ideational disturbance', and physical signs. Items are measured on a 3-point continuum: absent, mild or intermittent and severe. Nine or more points indicate a depressive disorder. It has been shown that the Cornell score was the best diagnostic scale for detecting depression in dementia.[15]

The number of falls in the past 1 month, the number of minutes spent in walking/exercise per week and the number of restricted activity days in the past 2 weeks (restricted activity is defined as spending more than half of the day in bed) were also recorded. Carer stress was measured by the Zarit Burden Interview.[16] It was designed specifically for the assessment of subjective burden of carers, defined as the extent to which carers perceived their emotional or physical health, social life and financial status to have changed as a result of caring for their relative with dementia.

All patients were assessed at baseline (0 month), 3, 6, 9, and 12 months post training. A physiotherapist and occupational therapist that was blinded to allocation groups conducted the assessments.

Statistical method

Between-group comparisons of baseline variables were conducted using the Chi-square test, t -test and Kruskal-Wallis test as appropriate. Longitudinal data on the primary and secondary outcomes was analysed by ANOVA with repeated measurements. A P value of <0.05 was considered statistically significant.

RESULTS

In all, 85 subjects were recruited; 49 (58%) received conventional treatment and 36 (42%) the exercise intervention. The mean age of the subjects was 76 (standard deviation [SD], 6) years, and 46 (54%) were female. Two patients (both in the control group) died during the study period; one died of a road traffic accident 9 months after entering the trial and one from chronic renal failure after 6 months. One patient refused to attend after 6 months.

The mean duration of illness was 2.9 (SD, 2.0) years. Among the disease categories, 52 (61%) had Alzheimer's disease (AD), 17 (20%) had vascular dementia (VaD), 14 (17%) had mixed dementia and 2 had Parkinson's disease dementia. The most frequent concomitant medical problems were: hypertension (41%), diabetes (25%), stroke (9%) and ischaemic heart disease (8%). About half (54%) were receiving cholinesterase inhibitor treatment. Only 13 (15%) of the subjects were attending day care centres regularly. The median MMSE and ADAS-Cog scores were 20 and 24, respectively.

There were no statistically significant differences between exercise and conventional treatment groups with respect to baseline characteristics (**Table 1**), except that more of the former were in receipt of cholinesterase inhibitor treatment (69% vs. 43%, p=0.017). The MMSE score diminished with time in both the exercise (p<0.001) and control (p<0.001) groups, but there was no significant difference between them. Similarly there was a reduction in ADAS-Cog scores with time in either group; the exercise intervention group enjoyed no advantage compared to the controls in this respect (**Table 2**). There was no significant difference in the rate of cognitive decline in patients with or without Alzheimer's dementia. There was no statistical significant trend in the Cornell Scale for depression in Dementia in the exercise group, but the subjects were less depressed in the control group at 3 months (p=0.004) and 12 months (p=0.027).

There was no significant trend in the physical component score on the SF-12 with time, and no significant differences between the exercise and control groups. There were improvements in the mental component scores in the SF-12 at 9 months (p=0.001) and 12 months (p=0.034) in the exercise group. However there were no statistically significant differences between the two groups with respect to changes with time.

Carer stress increased with time as reflected by a high Zarit Burden Interview score in the treatment group (p=0.002 for linear trend), while in the control group, the Zarit score increased at 9 and 12 months only. However there was no significant difference between the two groups.

In the exercise group, there was a significant

Table 1
Baseline characteristics

Characteristics	Exercise group (n=36)	Control group (n=49)
Mean (SD) age (years)	75 (7)	78 (6)
% of female	426%	63%
Mean (SD) duration of dementia (years)	2.58 (1.77)	3.06 (2.19)
% on cholinesterase inhibitor treatment*	69%	43%
Type of dementia		
Alzheimer's disease	66%	57%
Vascular dementia	14%	24%
Mixed dementia	14%	18%
Parkinson's disease dementia	5%	0%
% attending day care centre	11%	19%
Median (IQR) SF-12 physical component score	47.6 (41.3, 52)	49.2 (42.4, 52.4)
Median (IQR) SF-12 mental component score	53.2 (46.4, 57.3)	55 (50.3, 58)
Median (IOQ) Cornell Scale for Depression in Dementia	8.5 (6, 13.75)	8 (6,12)
Median (IQR) Mini-Mental State Examination	20 (16, 22.75)	20 (16.6, 22.5)
Median (IQR) Alzheimer Disease Assessment Scale-Cognitive Subscale	23.5 (20, 32.75)	24 (17.5, 31)
Mean (SD) 6-minute walking distance (m)	245 (90)	264 (100)
Mean (SD) functional reach (cm)	19.7 (7)	19.9 (8.3)
Median (IQR) Berg Balance Scale	47 (41, 50.75)	48 (42, 53)
Median (IQR) Zarit Burden Interview	19 (4.36)	10 (3.29)

* p=0.017

Table 2
Mean change of Mini-Mental State Examination (MMSE) and Alzheimer Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) from baseline

Time	Mean (SD) change of MMSE from baseline		P value	Mean (SD) change of ADAS-Cog from baseline		P value
	Exercise	Control		Exercise	Control	
3 month	-1.06 (2.63)	-0.04 (2.18)	0.055	1.61 (7.23)	-0.14 (5.69)	0.24
6 month	-1.39 (3.10)	-0.7 (2.67)	0.28	3.03 (8.66)	1.83 (6.84)	0.46
9 month	-2.28 (3.63)	-1.33 (2.84)	0.18	3.72 (8.12)	3.5 (6.56)	0.89
12 month	-2.36 (4.11)	-1.24 (2.73)	0.14	6.03 (10.68)	5.52 (6.54)	0.8

improvement in the 6-minute walking distance at 3 months (net improvement of 38 metres [SD, 42], p<0.001) and 6 months (23 m [SD, 49], p=0.009) compared to baseline. However the improvement decreased with time and became non-significant after 9 months. In the control group, the 6-minute walking distance decreased with time. The difference in the improvement in the 6-minute walk between the 2 groups remained statistically significant throughout the entire study period (**Figure 1**).

There was improvement in the functional reach scores in the exercise group with time, which was also significantly different from corresponding score patterns in the control group; the effect persisted at 12 months (**Figure 2**).

For Berg Balance Scale, there was significant improvement in balance performance compared to baseline in the exercise group, but the effect became non-significant at the end of 12 months (**Figure 3**).

When the study subjects were subdivided into the AD subgroup and mixed subgroup (AD + VaD group or VaD) the differences in 6-minute walking speed and Berg Balance Scale remained in favour of the exercise group in the initial 3 to 6 months in both the AD and mixed subjects. However for functional

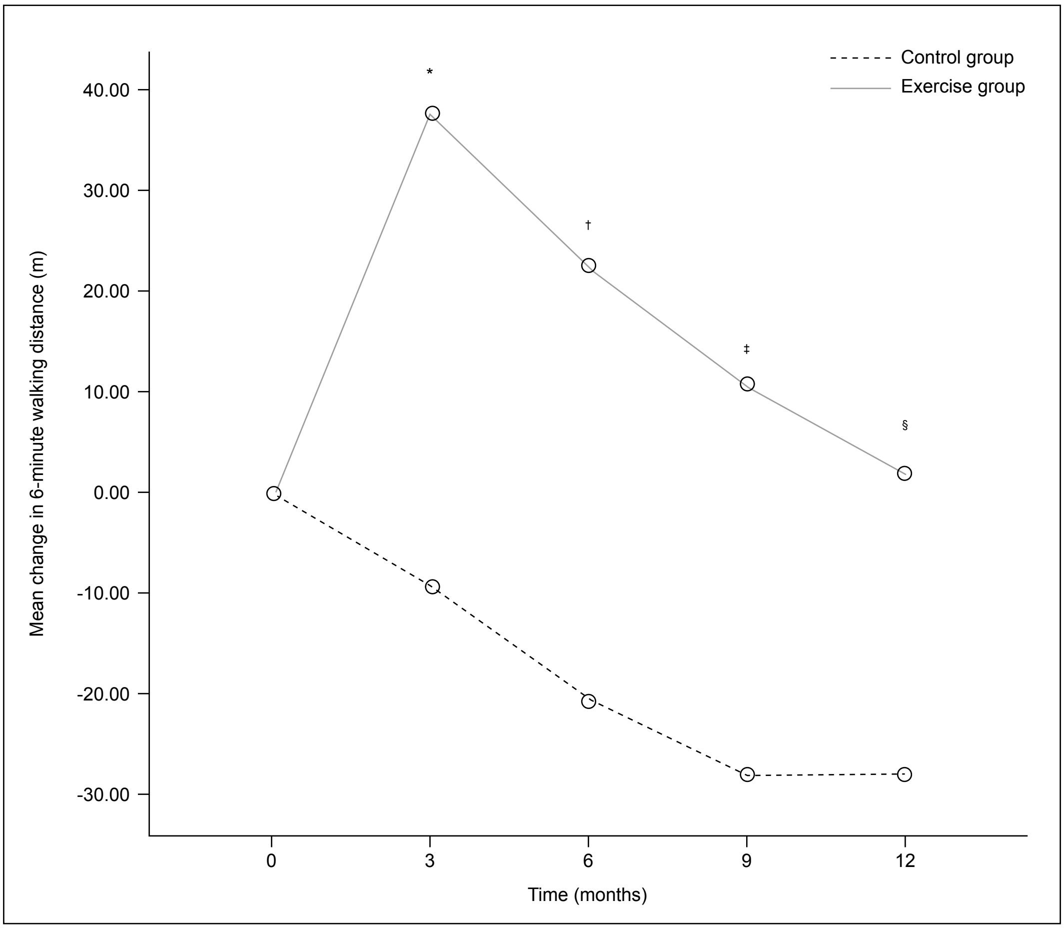

Figure 1. Differences in change from baseline in 6-minute walking test
* $p<0.001$
† $p<0.001$
‡ $p=0.002$
§ $p=0.014$

reach the mixed subjects enjoyed a significant improvement but not the AD subjects (**Table 3**).

The exercise group had less restricted activity days than the control group, especially in first 3 months of follow-up (mean difference 2.3, 95% confidence interval [CI] 0.2, 4.3).

DISCUSSION

Our study shows that the exercise programme significantly improved physical performances in dementia patients and the effect was sustained after 1 year. Subjects in the exercise intervention group were more active as reflected by a better walking speed in the 6-minute walking test, better flexibility and balance and fewer days of restricted activity. The annual rate of decline in mental function was around 1.5 in MMSE and 5 in ADAS-Cog scores. Thus, exercise was not shown to have a significant effect on cognitive function, as gauged by MMSE and ADAS-Cog scores. Although our study did not show any significant effect on cognitive function, the improvement in physical function was associated with better physical health and functional mobility in persons with dementia living in the community.

The MMSE and ADAS-Cog scores declined more in the intervention group, although the difference was not statistically significant. Also, more patients in the intervention group received cholinesterase inhibitor. It is not clear as to whether this was due to more rapid cognitive decline in the latter group, and consequentially more resort to such treatment. Nor do we know whether this group of subjects may have had more advanced dementia and therefore cognitively did not response well to exercise intervention. A longitudinal study on the outcome on this group of patients is suggested to monitor the rate of their cognitive decline.

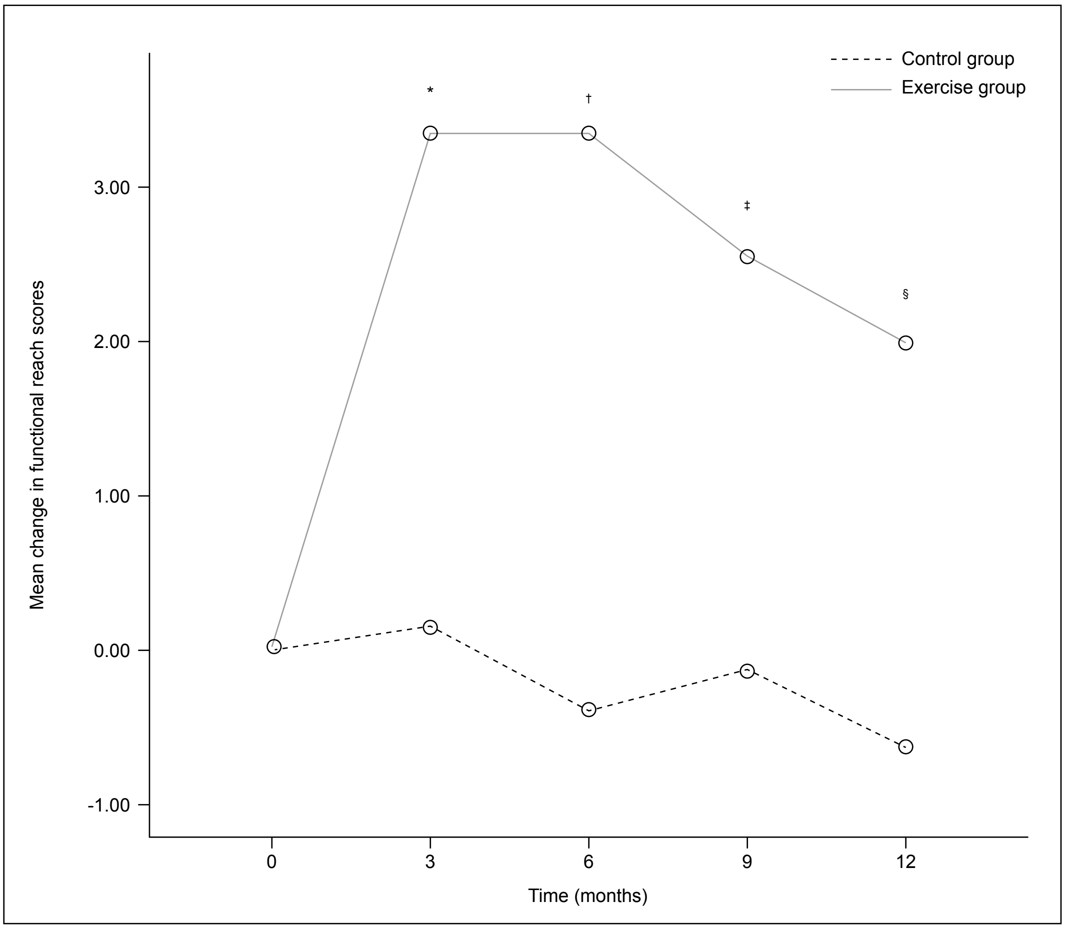

Figure 2. Differences in change from baseline in functional reach
* $p=0.007$
† $p<0.001$
‡ $p=0.019$
§ $p=0.009$

Non-pharmacological randomised controlled trials on patients with dementia are rare.[17-19] Previous studies on exercise intervention in older adults have not specifically targeted people with cognitive impairment,[8] have excluded older people who were not able to cooperate and were cognitively and behaviourally dysfunctional,[3,20,21] or included older adults with multiple health conditions.[22] It is well known that dementia affects cognition, emotional and behavioural functioning.[23] There are a number of studies linking dementia with physical deterioration. Alzheimer's disease patients show more signs of under-nutrition, higher risk of falls and fractures,[24] and decline more rapidly when judged by measures of mobility.[25] Alzheimer's disease patients who become injured are at a greater risk of subsequent injury and associated loss of independence than age-and-sex-matched controls.[26] Consequently, improved physical conditioning for dementia patients may extend their independent mobility and enhance their quality of life, despite progression of disease.

Although the rate of decline in cognitive function in the intervention group was greater than in the controls, the difference did not reach statistical significance. However, it has been postulated that physical exercise may have a protective effect, by slowing down mental deterioration. A larger scale study may be needed to investigate this possibility.

The finding that exercise training resulted in improved health-related physical functions in demented subjects is encouraging. Studies have shown that regular exercise is associated with a delay in the onset of dementia and Alzheimer's disease[27] in elderly persons. The positive effect of exercise training highlights the need to further understand the role of exercise on brain function and the development of dementia.

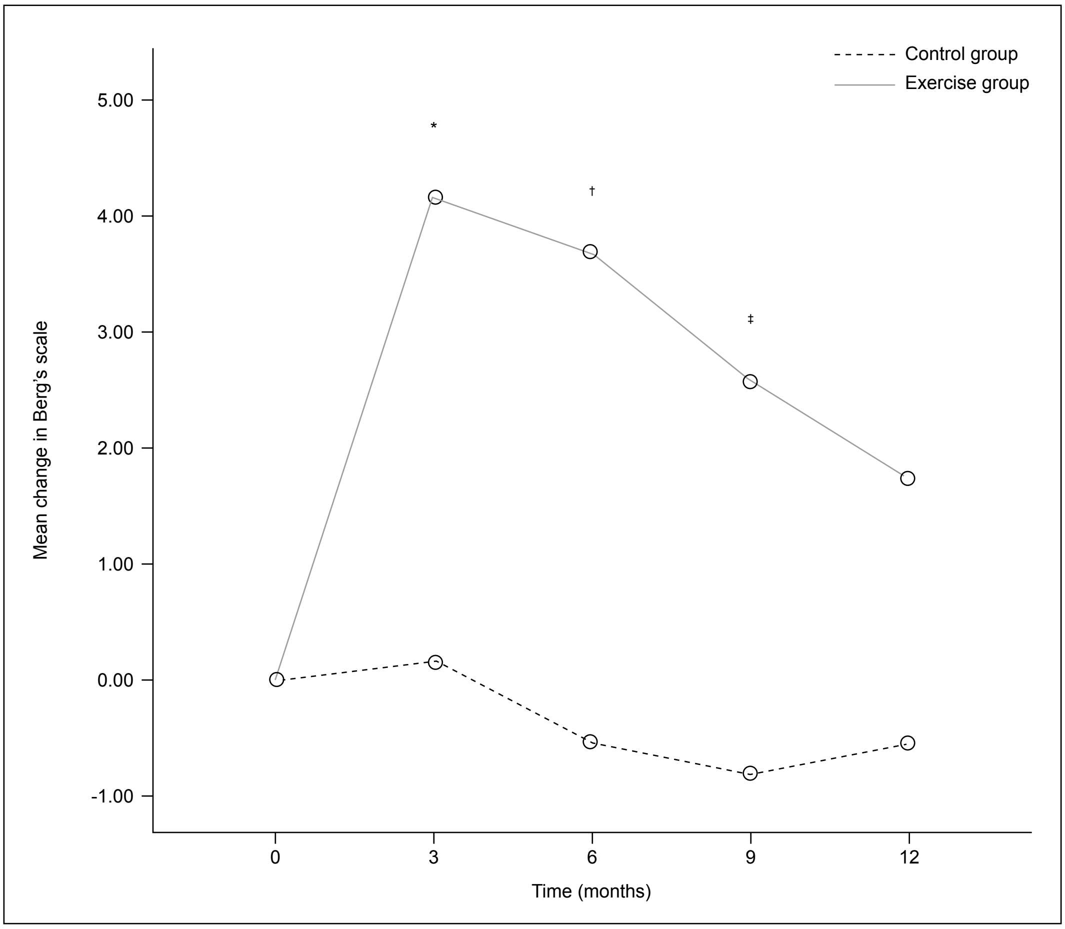

Figure 3. Differences in change from baseline in Berg's scale
* p<0.001
† p<0.001
‡ 0=0.003

Our study showed that the exercise programme was safe. No fall or exercise-related injury was reported during the 1 year of follow-up. The majority of studies on the effect of exercise on dementia patients were either home based[28] or depended on self-reported physical activity.[27] In this study a supervised training programme was specifically designed for dementia subjects and carried out in a geriatric day hospital. This ensured strict adherence and guaranteed intensity and duration of exercise. Whether offering more exercise sessions would have led to better results warrants further investigation. There was only one defaulter among the study subjects; the adherence to this type of exercise programme was high. However, additional training sessions may result in lower adherence. Exercise adherence was a significant predictor of change in activity of daily living (ADL) score.[29] The problem of adherence to high exercise intensity or duration needs more study.

Improvement in the 6-minute walking test means a better walking speed. A better walking speed may translate to improved physical function with some effect on improving ADL. The ADL (a key index of quality of life) affects the cost of caring for people with dementia.[30] This study demonstrated that exercise sessions twice a week could slow down deterioration in ADL and physical function in demented older people living in the community.

We found carer stress increased with time. This may be due to mental functions of the subjects deteriorating, and imposing more stress on the carer. Therefore in management of patients with dementia, health professionals should not only focus on the patient. More attention should be paid to the carer and the variety of stresses they encounter in taking care of their demented relatives, and resources should also be made available for this purpose.

Table 3
Mean change of physical performances from baseline

Physical performances	Mean (SD) change from baseline		
	Exercise group	Control group	P value
Vascular dementia and mixed group			
6-minute walk at 3 month (minute)	28.4 (26.1)	-9.3 (45.8)	0.022
6-minute walk at 6 month (minute)	10.8 (25.4)	-22.1 (29.3)	0.005*
6-minute walk at 9 month (minute)	2.96 (30.2)	-26.8 (34.1)	0.027
6-minute walk at 12 month (minute)	-11.2 (34.5)	-28.6 (26.9)	0.141
Berg's scale at 3 month	4.6 (3.2)	0.14 (2.3)	<0.001*
Berg's scale at 6 month	3.8 (3.5)	0 (2.2)	0.001*
Berg's scale at 9 month	2.8 (5.2)	-0.75 (2.2)	0.013
Berg's scale at 12 month	2.3 (5.9)	-0.4 (2.3)	0.191
Functional reach at 3 month (cm)	5.6 (3.9)	0.6 (3.5)	0.001*
Functional reach at 6 month (cm)	5.1 (4)	0.6 (2.9)	0.002*
Functional reach at 9 month (cm)	4.2 (5.8)	0.6 (3.5)	0.044
Functional reach at 12 month (cm)	4 (4.3)	0.15 (2.9)	0.024
Alzheimer's disease group			
6-minute walk at 3 month (minute)	43.7 (46.2)	-4.2 (37.3)	<0.001*
6-minute walk at 6 month (minute)	27 (57.7)	-18.8 (63.2)	0.01*
6-minute walk at 9 month (minute)	16.3 (70.3)	-28.7 (55)	0.016
6-minute walk at 12 month (minute)	13 (66.7)	-27.4 (57)	0.027
Berg's scale at 3 month	4.3 (2.6)	0.18 (3.1)	<0.001*
Berg's scale at 6 month	3.5 (4)	0.9 (7.5)	0.013
Berg's scale at 9 month	2.4 (5.5)	-0.9 (6)	0.048
Berg's scale at 12 month	1.4 (7.6)	-0.7 (6.1)	0.29
Functional reach at 3 month (cm)	1.9 (6.6)	-0.1 (2.6)	0.151
Functional reach at 6 month (cm)	2 (3.6)	-1.1 (5.1)	0.015
Functional reach at 9 month (cm)	1.3 (5.6)	-0.7 (3.9)	0.136
Functional reach at 12 month (cm)	0.7 (4.9)	-1.2 (3.7)	0.121

* p<0.0125 is significant

There are limitations to this study. The sample size was relatively small. The major barrier to the recruitment of subjects was the availability of carers. The majority of the patients depended on their carer to bring them back to our centre for training and assessment. Since most of the carers had other work, they could not afford free time to bring their relatives back on weekdays for training and assessment. Furthermore, we did not assess the potential outcomes of treatment on caregivers' satisfaction. Nor did we investigate the relative efficacy of exercise intervention in producing the results herein. Future research is needed to determine whether the effects obtained in this study can be replicated or improved. Due to limitation of resources, only 3 months of exercise training could be offered to our dementia subjects. This relatively short period of training may not be sufficient to bring about a significant change in cognitive function. A larger-scale study with a longer training period is suggested for the future.

CONCLUSION

It is well known that dementia is one of the most-feared illnesses of ageing, and people frequently cite it as a reason for not wanting to get old. They do not want to lose their independence and quality of life as a consequence of ageing.[31] Exercise has a positive effect on older patients with dementia and results in a significant improvement in physical function. Physicians and health promotion programmes might make use of these results to find effective ways to promote physical activity for all its well-known benefits, not only in healthy elderly people, but also in dementia patients.

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