

Feasibility of Recruiting and Assessing Health-Related Quality of Life and Physical Function in Older Chinese Adults with Cerebral Infarction

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Abstract: Objective: While it is known that exercise therapy can improve physical and emotional function in cerebral infarction (CI) patients, few studies have examined how well this would be accepted by older adults in China. **Methods:** In this study, the feasibility of recruiting and assessing health-related quality of life and physical function in older Chinese adults with cerebral infarction was assessed. Specific aims of the study were to evaluate the feasibility of recruiting older adults, with and without CI, from three different locations/settings in China; Compare the quality of life and physical function measures between CI and control subjects; Propose future larger randomized controlled studies of aerobic and resistance exercise training in both human and animal models after CI. **Results:** Overall, 66/275 (24.0%) surveys that were sent to older Chinese adults were returned and evaluated. Of those surveys returned, 18 (27%) met the study inclusion and exclusion criteria. Consequently, the results of this feasibility study indicate there is a recruitment yield (number of subject contacted/number of subjects who qualified for study) of 6.5%. These number varied at the different sites/settings, but the highest recruitment yield was seen in hospitalized patients. Despite small sample sizes, there were statistically significant differences in health-related quality of life and physical function between CI patients and control subjects. **Conclusion:** This feasibility study demonstrated that it is possible to successfully recruit CI patients for an exercise intervention study as well as to perform important assessments of health-related quality of life and physical function. Further randomized controlled trials, in humans and animal

models, will be needed determine if aerobic and/or resistance exercise training can improve health and physical function in older CI patients. Additional studies will be needed to determine the specific mechanisms responsible for the benefits seen with aerobic and resistance training.

Keywords: Feasibility; Quality of Life; Physical function; Cerebral Infarction; Exercise Therapy

Publication date: November, 2020

Publication online: 30 November, 2020

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1 Introduction

Cerebrovascular disorders account for 11.8% of the world-wide deaths each year^[1] and have an early recurrence rate of 8.56%^[2]. The most common type of cerebrovascular disorder is a cerebral infarction (CI).^[3] Cerebral infarction, sometimes also referred to as an ischemic stroke, happens when the cerebral artery is occluded due to atherosclerosis and/or thrombosis (blood clot). This causes interruption or paucity of blood flow to the brain, causing necrosis (cell death) and damage/dysfunction to specific regions the brain. Cerebral infarction is especially prevalent in older adults^[4]. In 2015 alone, there was 600,000 cases of CI worldwide^[5]. Cerebral infarction generally results in poor quality of life and reduced physical function. With the aggregating trend of an aging population, it is expected that the prevalence of CI will continue to increase and become a greater public health problem.

Although exercise has not been widely used in

the rehabilitation of CI patients, recent studies have determined that 30 to 60 minutes/day of moderate-intensity aerobic exercise can reduce the risk of colon and breast cancer and can effectively prevent diabetes, cardiovascular diseases, obesity and loss in cognitive function^[6]. A review of 19 studies has also shown that aerobic exercise programs, similar to cardiac rehabilitation programs, can improve endurance and walking capacity^[7]. While less is known about the benefits of resistance exercise training^[8], the use of weights and/or resistance bands^[9] have been shown to lower blood pressure, blood lipids, as well as a reduce of visceral fat and improve sleep quality.^[10] Another study determined that lifting weights for ~ hour/week can reduce the risk of stroke or heart attack by 40 to 70 percent. Moreover, it has also been revealed that resistant exercise training may reverse cellular aging by reducing the shortening of telomeres^[11].

Unfortunately, there have been very few studies investigating the overall effect of exercise interventions on health^[12] and specifically comparing aerobic exercise versus resistance training^[13] in older Chinese adults. Moreover, no studies to date that have examined the benefits of aerobic or resistance exercise on the quality of life and physical function in older Chinese adults that have had a experiences a CI. Consequently, this feasibility study was performed to gain a greater understanding on how to recruit and evaluate quality of life and physical function CI patients, as well as to determine patient's willingness to participate in an exercise intervention program. Results of this study will be very informative and instrumental in designing larger efficacy studies in CI patients. Specific aims of the study were to 1) evaluate the feasibility of recruiting older adults, with and without CI, from three different locations/settings in China, 2) compare quality of life and physical function assessments between CI and control subjects, 3) propose future larger randomized controlled studies of aerobic and resistance exercise training in both human and animal models after CI.

2 Methods

2.1 Study Overview

This study explored the feasibility of recruiting older Chinese adults with a history of cerebral infarction for an exercise therapy program (aerobic and resistance exercise). This study attempted to recruit

participants from three different recruitment locations and evaluate health status through general and disease specific questionnaires and physical function tests. Moreover, this study will assess the percentage of people that meet study inclusion and exclusion criteria and have a willingness to engage in exercise intervention program.

2.2 Recruitment of Study Participants

Potential participants in this study were recruited from three different sources/locations in China. Subjects in Group 1 were recruited from a "convenience" sample that was obtained through online and "word of mouth" communication. Subjects in Group 2 were recruited from a major Senior Home (YiYuan) in Guangdong, China. In this location, the study was introduced to potential participants through a questionnaire that was sent to all inhabitants in this facility. Those interested in participating completed the questionnaire and returned it to their respective nurse attendant. Subjects in Group 3 were recruited from three different prestigious hospitals in China: Xi'an Railway Primary Hospital, Xi'an Jiaotong University's First Affiliated Hospital, and Hong Kong University Shenzhen Hospital. The questionnaires were offered to prospective patients by the doctors in the Cardiovascular Department of each hospital. Those willing to participate in the study completed the questionnaires and provided their contact information and consent to use their medical information.

2.3 Study Inclusion and Exclusion Criteria

Inclusion criteria for this feasibility study included: 1) age >50 years; 2) willingness to provide self-reported CI history as well other medical information; 3) willing to participate in an exercise intervention; 4) willing to answer questionnaires and participate in physical function assessments. Exclusion criteria included: 1) regular exercise (>30 minutes multiple times per week); 2) hemorrhagic stroke; 3) self-reported physical impairment or condition that may influence the subject's ability to participate in exercise interventions or assessments required in the study; 4) refusal or other condition that may preclude them from giving written informed consent to the study; 5) having been instructed by medical professional to avoid intensive exercise or movement within the past year of the study. Before data collection occurred, each participant signed a form indicating

that the medical information obtained in this study was only for this research study and would not be used for any other purpose. Participants privacy was also maintained as the questionnaires and physical function data were obtained and coded by number and not personal information.

2.4 Efficacy Measures

2.4.1 Health-related Quality of Life

Health-Related Quality of Life is a standard measurement of an individual's or group's perceived physical and mental health over time. It measures the "well-being", an integration of mental and physical health, in order to approach disease prevention and health promotion in a more holistic approach. This measurement is unique in that it evaluates an individual's health and well-beings from his/her own perspective, allowing medical treatments to be at its most effective usage in satisfying the patient^[14]. Questionnaires used in this feasibility test are SF-36 health survey, a generic measurement of health status, as well as a Stroke-Specific Quality of Life (SS-QOL). The SF-36 Health Survey contains 36 questions, with eight-scale profile of scores as well as summary physical and mental measures. It doesn't target any specific population, differentiated by factors such as age, gender, ethnicity or disease diagnosed. This survey can help evaluate the subject's condition in a generic scale^[15]. Conversely, the Stroke-Specific Quality of Life targets stroke-diagnosed patients only. This survey will yield a more specified result in the study since it is disease-specific for stroke and considers the subject's conditions more holistically.^[16] Lower score for SF-36 test implies better fitness and health status

whereas the opposite is true for the stroke-specific quality of life assessment.

2.4.2 Short Physical Performance Battery

The Short Physical Performance Battery test measures the subject's physical function. It measures simple movements such as standing and walking and is usually adopted in rehabilitation programs to evaluate recovery of patients. It contains 3 sub-tests (including balance test, gait speed test, and chair stand test) and is scored from a scale 0-12 points, with each sub-test accounting for 4 points. A score of 12 indicates great physical movement capabilities while a 0 indicates minimal movement capabilities^[17].

2.5 Analytical Plan

In addition to determining means and standard deviations for the participant characteristics, the Mann-Whitney U test was used to determine if there were statistical differences between CI and control subjects on general and stroke-specific measures of health related quality of life and for the Short Physical Performance Battery (SPPB). Statistical significance was set a $P < 0.05$.

3 Results

Overall, 66/275 (24.0%) surveys were returned and evaluated. Of those surveys returned, 18/66 (27%) met the study inclusion and exclusion criteria. Consequently, the results of this feasibility study indicate there is a recruitment yield (number of subject contacted/number of subjects who qualified for study) of 6.5%. This number varied at the different sites/settings.

Table 1. Description of the Participants at Each Location

	Subject Group 1 (Convenience Sample) (<i>n</i> =18)	Subject Group 2 (Senior Home) (<i>n</i> =20)	Subject Group 3 (Hospital) (<i>n</i> =18)
Age	68.0 + 13.2	65.5 + 6.4	63.7 + 7.9
Gender (Male/Female)	7/11	11/9	8/10
Body Mass Index	25.6 + 2.7	29.1 + 6.7	24.3 + 1.8
Ethnic Distribution (Han/Man)	17/1	20/0	18/0
Systolic Blood Pressure	136 + 17	127 + 9	127 + 13
Diastolic Blood Pressure	72 + 9	84 + 8	83 + 6
Exercise Frequency	74.2% + 41.7%	50.2% + 45.2%	30.0% + 42.4

Data are presented as mean + SD or number/percentage
Exercise Frequency was calculated by minutes of Exercise per day*100%

In Group 1 (Convenience Sample), 25 questionnaires were sent out and 20 (80%) were returned. Among the surveys returned, all 20 participants were willing to enroll in the study and follow the exercise intervention recommendation. Two participants were unable to perform physical assessment due to paralysis/physical handicap. Among the other 18 participants, two (11%) met the inclusion/exclusion criteria and were enrolled into the study. Both subjects were females that aged 52 and 82 years.

In Group 2 (Senior Home Sample), 200 questionnaires were sent out and 22 (11%) were returned. Among the 22 surveys received, all 22 (100%) participants were willing to enroll in the study and follow the exercise intervention recommendations. Two of the participants were < 50 years of age and thus were excluded. Among the eligible 20 participants, three (15%) met the inclusion/exclusion criteria and were enrolled into the study. One of the subjects was a 79-year-old female and the other two were males aged 72 and 76 yrs.

In Group 3 (Hospital Sample), 50 questionnaires were sent out and 24 (48%) were returned. Twenty-four (100%) of those that returned the questionnaires were willingness to participate in the study, including performing physical assessment and following the exercise intervention recommendations. Among the 24 participants, six (25%) were excluded due to age < 50 ($n=2$) and ($n=4$) who were physically unable to participate in an exercise intervention or perform the physical assessments. Finally, the average age of the 13 (75%) that met inclusion/exclusion criteria was 65 yrs and 70% were male.

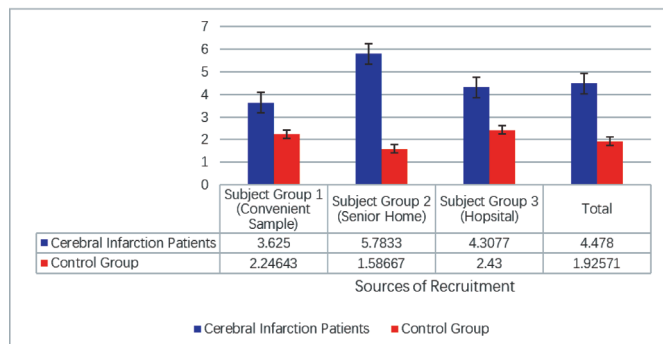


Figure 1. Average (SD) SF-36 Scores for the three sources of recruitment comparing cerebral infarction patients versus control subjects

Figure 1 reveals noticeable differences in the SF-36 scores between cerebral infarction patients and the control group in all three recruitment groups. However, the Mann-Whitney Statistical Test (see table 2) indicated there were no statistically significant differences between the CI and control groups at any of the three locations/settings.

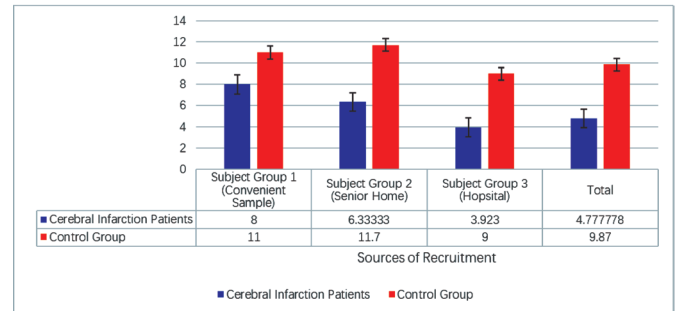


Figure 2. Average (SD) Stroke-Specific HRQOL Scores for the three sources of recruitment comparing cerebral infarction patients versus control subjects

Figure 2 reveals noticeable differences in Stroke-Specific HRQOL scores between cerebral infarction patients and the control group in all three recruitment groups. However, the Mann-Whitney Statistical Test (see Table 2) indicated there only a statistically significant differences between the CI and control groups in the hospital sample

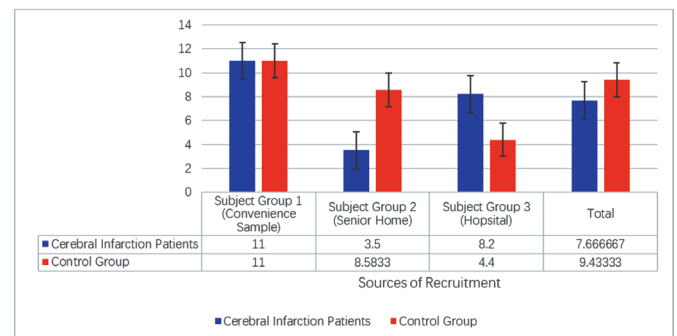


Figure 3. Average (SD) Short Physical Performance Battery Score for three sources of recruitment comparing cerebral infarction patients versus control subjects

Figure 3 reveals potential differences in SPPB scores between cerebral infarction patients and the control group. Although there was no differences observed in group 1 (convenience sample) the Mann-Whitney Statistical Test (see Table 2) indicated there was a statistically significant difference in SPBB scores between the CI and the control group in the hospital sample

Table 2. Significance level (p-value) between group (CI vs. CON) in each location/setting determined by Mann-Whitney U-Test.

	SF-36 Score	Stroke specific QOL Score	SPPB Score
Group 1 (Convenience)	0.29	0.23	0.50
Group 2 (Senior Home)	0.07	0.08	< 0.01*
Group 3 (Hospital)	0.24	< 0.01*	< 0.01*

*Significant difference between CI versus Control ($P < 0.5$)

4 Discussion

This feasibility study was performed to gain a greater understanding on how effectively researchers can recruit and evaluate quality of life and physical function in CI patients, as well as to determine patient's willingness to participate in an exercise intervention program. Results of this study will be very informative and instrumental in designing larger efficacy studies in CI patients. As stated earlier, the specific aims of the study were to 1) evaluate the feasibility of recruiting older adults, with and without CI, from three different locations/settings in China, 2) compare quality of life and physical function assessments between CI and control subjects, 3) propose future larger randomized controlled studies of aerobic and resistance exercise training in both human and animal models after CI. As seen in Table 1, the participants at the three different locations/setting has similar descriptive characteristics.

4.1 Aim 1

To evaluate the feasibility of cerebral infarction patients within the limit of our proposed inclusion and exclusion criteria, a total of 275 surveys were sent out to prospective subjects at the three different locations/settings. Overall, 66 (24.0%) surveys were returned and evaluated. Of those surveys returned, 18 (27%) met the study inclusion and exclusion criteria. Consequently, the results of this feasibility study indicate there is a recruitment yield (number of subject contacted/number of subjects who qualified for study) of 6.5%. This number varied at the different sites/settings. While the survey return rate was highest (80%) in the convenience sample (Group 1), the recruitment yield was low (11%) due to large number of subjects that did not meet the inclusion/exclusion criteria. In comparison, the response rate (11%) and the yield rate (15%) where both low for the Senior Home (Group). Finally, the response

(48%) and recruitment yield (75%) was best at the hospital setting. This is likely due to the high number of patients that had CI and the involvement and influence of medical doctors at this location/setting.

The most common reasons for subjects declining participation in the study included: lack of time to adhere to an exercise intervention program, fear of injury/illness or unwillingness to perform exercise and physical assessments, and concerns over confidentiality of medical information. These concerns must be addressed if investigators expect to increase recruitment yield for future studies.

4.2 Aim 2

As seen in Table 2,3,& 4, there are meaningful differences between CI patients and control subjects in general and stroke-specific quality of life and physical function measures. However, the small sample sizes of the CI groups make statistical comparisons difficult. Despite this limitation, this study provides objective evidence that that general and disease-specific quality, as well as physical function (SPPB), lower in CI patients compared to control subjects. Consequently, it will be important to determine if exercise interventions will be able to improve health-related quality of life and physical function in CI patients.

4.3 Aim 3 Future Directions.

4.3.1 Human Exercise Training Study

The present study indicates that it is generally feasible to recruit older adults in China with a history of CI for an exercise intervention. Subsequently, the future direction of this research is to conduct a study evaluating the effect of aerobic exercise and resistant training on this patient population. Specific aim of this future research is to: 1) compare the effects of aerobic exercise versus resistance type exercise on quality of life and physical function measures (same measures made in this feasibility study) 2) to determine if the source/location of recruitment (CI patients in the community, senior home, hospital) has a differential effect on the benefits obtained from the exercise interventions.

Among each source of recruitment (convenient sample, senior homes, and hospitals), participants will be randomly assigned to four different aerobic exercise and resistant training intervention. Group 1 will perform aerobic exercise only; Group 2

will perform resistant training only; Group 3 will perform both aerobic exercise and resistant training; and group 4 will serve as the control group and not perform any exercise above their current levels. Subjects assigned to aerobic exercise only will perform aerobic exercise four times per week. Each session will last approximately 35 minutes, in the order of five-minutes warm-up, ten-minutes walking/jogging, five-minutes rest, ten-minutes walking/jogging, and five-minutes cool down. Subject assigned to resistant training only will be expected to follow the same routine except that the aerobic exercise will be replaced by resistance exercise using elastic band/hand weights. Subjects in Group 3 will perform aerobic exercise two times/week and the resistant training routine two times per week. To enhance adherence, each participant will determine the location, time of the day, and day of the week that is best for them.

4.3.2 Rodent Exercise Training Study

In addition to conducting studies on humans, it will also be important to examine the effect of aerobic exercise and resistant training on in animal models. Thus, another future direction of the feasibility study is to perform experiments comparing the effect of aerobic exercise and resistant training on rodents with induced CI. The specific aim of this experiment is to compare the difference between aerobic exercise and resistant training's effect on cerebral infarction rodents.

The aerobic exercise intervention will be implemented by letting the rodent subjects run on a constructed running wheel. The running wheel will have a motor attached, set to a specific speed and turned "on" for a specific amount of time, to ensure the amount of designated aerobic exercise was performed. There will also be water on each side of the wheel to prevent the rodents to jump off the wheel and to avoid the aerobic exercise intervention. Moreover, the resistance training intervention will be implemented by tying small weights onto the paws of the rodents for designated time-period while they are in active motion. Though the weight tied will not be great, the lower exercise intensity between the two groups of rodents will be compensated by longer time period of the later. Though the weight tied onto the paws of the rodents will be small, the exercise intensity between the two groups of aerobic exercise

and resistance training will be kept approximately equal by lengthening the time period of the resistance training exercise intervention. The effect of the exercise intervention will be measured by recording the blood pressure, observing the activity of the mice, and thus computing its recovery.

5 Conclusion

This feasibility study, conducted at three different locations/setting in China determined that it is possible to successfully recruit CI patients for an exercise intervention study as well as to perform important assessments of health-related quality of life and physical function. Further randomized controlled trials, in both humans and animal models, will be needed determine if aerobic and/or resistance exercise training can improve health and physical function in older CI patients. Additional studies will be needed to determine the specific mechanisms responsible for the benefits seen with aerobic and resistance training.

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