Evaluating the effectiveness of stepwise swallowing training on dysphagia in patients with Alzheimer's disease: a study protocol for a randomized controlled trial

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Research Article

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Abstract

***Background**:* The high prevalence of dysphagia among Alzheimer's diseases (AD) has incurred many negative impacts. Therefore, effective and practicable dysphagia treatment are needed. As a fundamental rehabilitation of dysphagia, swallowing muscles exercises have received increased attention. Stepwise swallowing training (SST), integrated all swallowing organs movement, is expected to improve swallowing dysfunction among AD patients. By using randomized controlled trial design, the proposed study conducts a multi-center research to evaluate the effectiveness of SST program among AD patients.

***Methods**:* A multi-center randomized controlled trial, with a 4-week follow-up period after intervention, will be conducted among psychiatric hospitals in Guangdong, China. Participants in the control group will be assigned to routine dysphagia care, participants of the intervention group will undergo the same nursing care while additionally receive SST program. The SST program includes five sections of swallowing organs training: lip movement, facial movement, tongue movement, mandibular movement, and neck movement, respectively. Primary outcomes evaluate the swallowing function, including Water Swallowing Test (WTS) and Standard Swallowing Assessment (SSA). Secondary outcomes aim at measuring the improvement of negative impacts of dysphagia, including eating behavior, ability of daily activity, and nutritional status. Data will be collected at baseline (T_0), at 2 weeks (T_1, intervention completed), and at 4 weeks after intervention (T_2, follow-up).

Discussion: This study will offer trial-based evidence of the effectiveness of SST in relieving dysphagia among AD patients. SST program is expected to improve both the swallowing function and reduce negative impacts of dysphagia, with exploration of acceptability in SST program.

Trial Registration: Chinese Clinical Trail Registry, ChiCTR2200056481. Prospectively registered on 6 February 2022, http://www.chictr.org.cn.

Background

Alzheimer's disease (AD) has become one of the largest global economic burdens. According to the 2015 World Alzheimer's Disease Report, the total global cost of dementia will increase at an annual rate of more than 40% between 2015 and 2030—from 818 billion dollars to 2 trillion dollars[1]. However, recent research suggested that China's domestic socio-economic burden has been overwhelmingly underestimated; this will significantly affect the estimated global cost. In 2015, the cost of AD in China has reached 1.47% of the Gross Domestic Product (GDP), while the worldwide cost accounted for 1.09% of the global GDP, indicating a higher socio-economic cost in AD patients in China. Morever, the annual cost of an AD patient in China was 19 144.36 US dollars (USD), and the annual social and economic cost of AD was 167.74 billion USD, which was 5.95 times higher than the estimated value in the aforementioned report. What's more, by 2030, total annual cost related to dementia will reach 50.749 billion dollars[2].

The high socioeconomic burden of AD is mainly due to caregiver demands. Caring for AD patients is highly challenging for their caregivers and family members. The primary difficulty in caregiver is caused by the decline in AD patients' daily-living ability, specifically, the swallowing dysfunction. Clinically, the swallowing dysfunction leads to malnutrition, dehydration, weight loss, fear of eating, and other complications; consequently, it might extend hospital stay and even cause severe injury or death in extreme cases[3]. Swallowing dysfunction or dysphagia, which is a group of clinical syndromes, can occur as a result of various diseases. Dysphagia refers to improper transfer of food from the mouth to the esophagus and the stomach, caused by the impairment of the swallowing organs (e.g., mandible, lips, tongue, soft palate, larynx, esophagus, and so on). Generally, the swallowing process includes the following four physiological stages: oral preparatory, oral, pharyngeal, and esophageal[4].

Significant attention is needed to address the high prevalence of dysphagia in AD patients. Previous studies indicated an incidence rate of 32–45% among mild AD patients with dysphagia, and 84–93% among moderate and severe AD patients. Abnormal swallowing function in AD patients manifested as weak tongue movement and pressure, generally occurring in the oral and pharyngeal stages of swallowing. Hence, due to abnormal swallowing function, individuals might exhibit delayed pharyngeal reflex, reduced pharyngeal muscle strength, and food residue after swallowing. Individuals with abnormal swallowing function experiencing difficulty in forming and pushing the food bolus, and hence, are at high risk of food aspiration[5].

Studies have reported that AD patients with dysphagia at admission are at a higher risk of malnutrition than those without dysphagia, which is associated with respiratory infection and increased mortality[6]. When screened using the Water Swallowing Test, the incidence rate of malnutrition was 1.67 times higher, with which the severity of dysphagia was positively correlated. Besides, malnutrition also reduces the quality of life in patients[4]. A multi-center cohort study found that swallowing dysfunction was an important cause of pneumonia and lower respiratory tract infection in 170 elderly people in a nursing home (OR = 2.000, 95%CI = 1.2–3.3, P = 0.10)[7]. Thus, optimal solutions are urgently needed to improve patients' swallowing function and living ability.

Dysphagia treatment includes three approaches: compensatory strategies, swallowing rehabilitation, and other approaches. The first aims to reduce the effects of impaired bolus flow to ensure the safety of oral diets[8]; it has many forms, such as postural adjustment, diet modification, swallow maneuvers, and enteral feeding. Changes in head or body posture are recommended to reduce aspiration or residue. Many postural techniques including (but not limited to) head down and lift, and side-lying, can successfully eliminate aspiration on at least one bolus volume of liquid[9]. Logemann et al. conducted a study using thin liquids with either chin-tuck or nectar-/honey-thickened liquids in individuals with dementia or Parkinson's disease (PD). Overall, fewer participants aspirated on nectar- ($p < 0.01$) and honey-thickened liquids ($p < 0.01$)[10]. While previous studies are conflicted about these strategies and some data suggest that postural adjustments are inferior to active rehabilitation, other approaches include chemo-denervation, pharmacological treatment, neuromuscular electrical stimulation, and non-invasive brain

stimulation[11, 12]. Chemical myotomy and drugs application are not highly recommended as first-line treatment in older adults with dysphagia due to the potential risks and side effects.

Wang et al. synthesized 27 randomized controlled trials to explore the effect of noninvasive neurostimulation therapies (repetitive transcranial magnetic stimulation [rTMS], transcranial direct current stimulation [tDCS], and surface neuromuscular electrical stimulation [sNMES]), which work through magnetic or electric fields to trigger and regulate the depolarization of cortical neurons, on dysphagia patients after stroke[13]. A positive effect of rTMS, tDCS, and sNMES was reported in the recovery of swallowing function (standardized mean difference = 0.91; 95% CI: 0.54–1.27; $Z = 4.84$; $P < 0.00001$; $I^2 = 86\%$). However, there is no recommended treatment protocol, and for implementation, a specific equipment is required[14].

Swallowing rehabilitation comprises exercises targeted to train specific muscles or muscle groups[8]. Given this development, more evidence-based therapeutic exercises were introduced—instead of centering on an isolated muscle, the training program gradually became more systematic and available. Kim et al. explored the instant effect of simple oral exercise (SOE), performed two times per day for a week, on 84 older adults. Masticatory performance improved immediately by around 16% in the poor-chewing group, and the unstimulated saliva production in all subjects increased to 0.26 ml/min immediately after SOE[15]. Kang et al. examined the impact of a bedside exercise program, which comprised oral, pharyngeal, laryngeal, and respiratory exercises. After implementing the program in 25 stroke patients for one hour per day for two months, the results showed a significant improvement, compared to the control group, in the swallowing function (at the oral phase) and depressive symptoms [16].

However, swallowing exercises, the fundamental rehabilitation for dysphagia, need more high-quality evidence regarding their implementation in AD. Under the neural regulation mechanism of the cerebral cortex sensorimotor, practicing swallowing exercises is effective for dysphagia with stroke/PD or older adults[17]. Clinicians find the implementation of appropriate rehabilitation exercises challenging in patients with AD. In China, clinicians apply swallowing exercises, such as lip lordosis and adduction, mandibular opening and closing, cheek blowing, and tongue extension, generally combined with routine care and other treatments. These exercises can be effective in increasing the flexibility and coordination of swallowing organs and improving the relevant muscles' strength. Nonetheless, whether swallowing exercises are effective in dementia is controversial. Therefore, simple and feasible swallowing rehabilitation training should be developed for patients with impaired cognition and attention deficit. Based on the current swallowing rehabilitation literature, a multi-center randomized controlled trial will be conducted in three mainland hospitals to investigate the effect of stepwise swallowing training on the function and daily-living ability in AD patients.

Objectives

Based on the literature and clinical evidence, a program has been developed to improve AD patients' swallowing function, from top to bottom—muscle training in lips, tongue, face, and neck. The study aims

to evaluate the effectiveness of the Stepwise Swallowing Training (SST) in swallowing function among AD patients with dysphagia.

Methods

Trial design

This training program is a multi-center, single-blinded, randomized controlled trial (RCT) with a six-week follow-up period. All stages are conducted according to the SPIRIT reporting guidelines[18]. Treatments administered will be allocated randomly according to a 1:1 ratio by an online random-number generator of SPSS software by research assistants who are not involved in assessment and intervention. The researcher will then offer the research assistants in each hospital of the allocation of groups with sequentially numbered opaque, sealed and stapled envelopes. Then, the training schedule will be conducted based on this research protocol.

Study settings and participants

This trial will be conducted in three major public psychiatric hospitals in Guangdong, China—Affiliated Brain Hospital of Guangzhou Medical University (GZ), the Third Hospital of Jiangmen (JM), and the Third Hospital of Yuebei (YB). This research has obtained ethical approval from the Institutional Review Board of GZ and it will be conducted with the consent of each hospital's executives. Before allocation, informed consent will be obtained from all participants.

Inclusion and exclusion criteria

A total of 100 participants of both sexes (women and men) aged above 60 years with AD will be recruited from the three main research institutes.

Inclusion criteria are: a) diagnosed as AD by DSM-5; b) score $\leq$ 25 on the Mini-mental State Examination (MMSE); c) score a third-degree or higher on the Water Swallowing Test, demonstrating a risk of aspiration[19]; d) have basic communication ability to complete the tests in this trial.

Exclusion criteria are: a) swallowing disorders caused by other organic diseases, such as oral disease, esophageal obstruction, digestive tract disease, tumors, or stroke; b) complications such as other serious somatic diseases that are not suitable for practicing swallowing exercises; c) serious impairment in hearing or vision, which may hinder following instructions.

Interventions

Participants in the control group will receive routine dysphagia care, While the intervention group will adopt SST based on routine care five times a week for two weeks. The process addresses five sections of swallowing muscles, and each section will provide step-by-step training, according to the difficulty experienced by the participant. Each section will be divided into three difficulties and start, each time,

from levels 1 through 2–3, as presented in Fig. 1. The instructional video will be shown to the patient along with one-to-one guidance.

Routine nursing care during intervention

During the intervention and follow-up, participants and their caregivers of both groups will being provided routine nursing care and health education about swallowing dysfunction. If the participants take medication that might affect the swallowing function, it will be recorded in case report form.

Outcomes

Primary outcomes have been identified as Standard Swallowing Assessment and Water Swallowing Test, which will be conducted to evaluate the main effects of the interventions with objective clinical indicators.

To assess the effectiveness of eating behaviors, daily activity abilities, and nutritional status, secondary outcomes include responses on the Abnormal Eating Behavior Questionnaire and the Mini-Nutritional Assessment- Short Form, Barthel Index, the safety of swallowing training, and the attendance rate. Safety will be calculated in terms of adverse effects (Safety = [the number of adverse events/the number of engaged participants * 100] %). The flow chart of this study will be presented in Fig. 2.

Sample size

The sample size was estimated by G*Power 3.1 using repeated measures. We set an alpha error of 0.05, a beta error of 0.05, and the effect size f = 0.25. After calculation, a total sample size of 72 was required. To accommodate for a 20% attrition rate and other confounding factors, we recruited 100 participants. After obtaining informed consent, each involved hospital was allocated into the intervention group and the control group in a 1:1 ratio.

Blinding

This is a single-blinded study. Participants will not be aware of the pattern of research allocation. The research assistants completing the surveys will not be involved in the swallowing training program.

Data collection and management

The impacts of swallowing training will be collected at baseline (T_0: enrollment), and at two weeks (T_1: the end of intervention) and four weeks after intervention (T_2: follow up). Other outcomes including the adverse events, attendance rate, and attrition rate will be continuously collected every two weeks from baseline. Research assistants will be trained together to ensure consistent results. Moreover, training videos and anime pamphlets will be given to family members and caregivers when participants are discharged from the hospital, and they will be contacted via telephone or WeChat to ensure the training process and measurements.

After the measurement, the data will be sorted and coded to eliminate invalid questionnaires. After the completion of data entry, the accuracy will be re-verified.

Statistical methods

Exploratory data analysis and Shapiro-Wilk tests will be performed to determine the normality of data distribution. Continuous variables will be expressed as means with standard deviations or medians with inter-quartile ranges; mean differences will be expressed from baseline to the end of the study. For categorical variables, counts and percentages will be presented, and between-group comparisons at baseline will be tested with the x^2 test [20]. Between-group differences at baseline, and in the change from baseline to the end, will be tested with repeated measure analysis of variance. An analysis of covariance will be used to adjust for baseline cognitive functioning. Paired t-tests will be performed for between-group comparisons from the baseline to the end. The level of significance will be set as a two-sided *P* value less than 0.05. Data analysis will be conducted using SPSS version 20.0 with intent-to-treat analysis (ITT) and per-protocol (PP) analysis. The results of the ITT analysis will be compared with those of the PP analysis to determine the consistency.

Study quality control

The validity and reliability of the instruments used in this study have been examined. The psychiatric hospitals involved in this study are qualified in research and geriatric mental care and can offer adequate support. To improve homogeneity, all research assistants will receive the unified training for proper assessments and check the questionnaire; the intervention will use standardized teaching videos and instruction. Moreover, the primary researcher will check the videos recorded during the intervention twice weekly for the performance adherence of patients and the staff.

Discussion

This protocol presents a multi-center RCT to assess the effectiveness of progressive swallowing exercises on the swallowing function, daily activity life, and eating behaviors in AD patients in Guangdong, China. The intervention program addresses five main swallowing muscle groups and will be taught stepwise.

Monitoring

Although the intervention in this study is neither invasive nor involving food usage, necessary side effects will be monitored by the researcher. To ensure compliance with the intervention program, a research assistant will be assigned to each hospital, who will be responsible for monitoring the program through recorded videos and providing biweekly progress reports, which include the assessment of training impact.

Risks, burdens, and benefits

The intervention will be implemented based on the patient's physical condition. The physical and emotional distress induced by the intervention (e.g., an increase in respiratory and heart rates) are assumed to fall within the range of a normal reaction. To reduce the discomfort during SST, research assistants will maintain participants' hydration and ensure appropriate rest. In a previous study, the Water Swallowing Test score and Barthel Index improved after intervention[21]. This study has been assessed by the ethical department in Guangzhou mental health center as a non-invasive program. Based on these assessments, the training program designed for dysphagia is not harmful for AD patients.

Before commencement, to avoid the risk of medical emergencies during the implementation, the nurses and research assistants will be instructed about the safety considerations and safety protocol. The caregivers or family members will respond to the questionnaire, while the participants will undergo the cognitive function test, that is, MMSE. Participation in the study will provide no direct benefit to the respondents.

Modification and inquiry

Any modification or inquiry regarding the study will be discussed through the Affiliated Brain Hospital of Guangzhou Medical University. During the study period, inquiries from the patients and their families will be gathered and solved by research assistants.

Confidentiality

The personal data including participants' names, addresses, telephone numbers, and so on contained in the consent form and case report form will be stored properly. All data will be anonymized using a research ID number when entered into computer storage.

Post-trial care

If the study demonstrates no negative effects, participants in the control groups will be invited to participate SST program after the study time-frame.

Dissemination policy

The results will be disseminated to professionals and hospitals in geriatric and mental care in Guangdong province. The findings will also be disseminated to peer reviewed scientific journals and presented at academic conferences.

Trial status

This manuscript describes the SST trial protocol version #1 dated February 6, 2022. Recruitment will begin in March 2022 and the anticipated completion is March 2023.

Abbreviations

GDP
Gross Domestic Product
SST
Stepwise Swallowing Training
RCT
Randomized Controlled Trials
MMSE
Mini-mental State Examination
ITT
Intention-To-Treat
PP
Per-Protocol

Declarations

Ethics approval and consent to participate

This research has obtained ethical approval from the Institutional Review Board of Affiliated Brain Hospital of Guangzhou Medical University (2021070). Written informed consent will be obtained from participants before the surveys.

Consent for publication

Not applicable.

Availability of data and materials

The datasets will be available from the corresponding author on reasonable request

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

CW, KZ, JY, and AX conceived this study. HY, HW, TW, LY, JG, and AX participated in sampling methods design. JY, LY and XZ participated in statistical methods design. CW, JY, XH, and AX drafted and revised this protocol. All authors had read and approved the final manuscript. CW, JY, and XH were listed as co-

first authors because they contributed equally to the study. AX, LY, and JG were assigned to be the corresponding author.

Acknowledgement

Not applicable

References

1. Alzheimer's Disease International. Wimo A, Wu GCAMGMPMP,Yu-Tzu: **World Alzheimer Report 2015-The Global Impact of dementia,an analysis of prevalence, incidence, cost and trends**. In: *Alzheimer's Disease International (ADI), London* 2015.
2. Jia L, Quan M, Fu Y, Zhao T, Li Y, Wei C, Tang Y, Qin Q, Wang F, Qiao Y, et al. Dementia in China: epidemiology, clinical management, and research advances. Lancet Neurol. 2020;19(1):81–92.
3. Jia J, Wei C, Chen S, Li F, Tang Y, Qin W, Zhao L, Jin H, Xu H, Wang F, et al. The cost of Alzheimer's disease in China and re-estimation of costs worldwide. Alzheimers Dement. 2018;14(4):483–91.
4. Kyle G. **Managing dysphagia in older people with dementia.**. British Journal of Community Nursing 2011.
5. Low J, Wyles C, Wilkinson T, Sainsbury R. The effect of compliance on clinical outcomes for patients with dysphagia on videofluoroscopy. Dysphagia. 2001;16(2):123–7.
6. Espinosa-Val M, Martín-Martínez A, Graupera M, Arias O, Elvira A, Cabré M, Palomera E, Bolívar-Prados M, Clavé P, Ortega O. **Prevalence, Risk Factors, and Complications of Oropharyngeal Dysphagia in Older Patients with Dementia**. Nutrients 2020, 12(3).
7. Loeb M, McGeer A, McArthur M, Walter S, Simor AE. Risk factors for pneumonia and other lower respiratory tract infections in elderly residents of long-term care facilities. Arch Intern Med. 1999;159(17):2058–64.
8. Di Pede C, Mantovani ME, Del Felice A, Masiero S. Dysphagia in the elderly: focus on rehabilitation strategies. Aging Clin Exp Res. 2016;28(4):607–17.
9. Logemann JA, Rademaker AW, Pauloski BR, Kahrilas PJ. Effects of postural change on aspiration in head and neck surgical patients. Otolaryngol Head Neck Surg. 1994;110(2):222–7.
10. Logemann JA, Gensler G, Robbins J, Lindblad AS, Brandt D, Hind JA, Kosek S, Dikeman K, Kazandjian M, Gramigna GD, et al. A randomized study of three interventions for aspiration of thin liquids in patients with dementia or Parkinson's disease. J Speech Lang Hear Res. 2008;51(1):173–83.
11. Manduchi B, Fainman GM, Walshe M. Interventions for Feeding and Swallowing Disorders in Adults with Intellectual Disability: A Systematic Review of the Evidence. Dysphagia. 2020;35(2):207–19.
12. Carnaby G, Hankey GJ, Pizzi J. Behavioural intervention for dysphagia in acute stroke: a randomised controlled trial. Lancet Neurol. 2006;5(1):31–7.

13. Wang T, Dong L, Cong X, Luo H, Li W, Meng P, Wang Q. **Comparative efficacy of non-invasive neurostimulation therapies for poststroke dysphagia: A systematic review and meta-analysis**. Neurophysiol Clin 2021.
14. Wan G, Zhang Q: **Clinical work guide for rehabilitation therapists for dysphagia** (**in Chinese**): Beijing: People's Medical Publisher; 2019.
15. Kim HJ, Lee JY, Lee ES, Jung HJ, Ahn HJ, Kim BI. Improvements in oral functions of elderly after simple oral exercise. Clin Interv Aging. 2019;14:915–24.
16. Kang J-H, Park R-Y, Lee S-J, Kim J-Y, Yoon S-R, Jung K-I. The Effect of Bedside Exercise Program on Stroke Patients with Dysphagia. Annals of Rehabilitation Medicine. 2012;36(4):512–20.
17. China Ecgfreatosdi. Expert consensus on evaluation and treatment of Swallowing disorders in China (2017 edition) Part II of treatment and rehabilitation Management (in Chinese). Chin J Phys Med Rehabilitation. 2018;40(1):1–10.
18. Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. BMJ. 2013;346:e7586.
19. Sadakane-Sakuramoto A, Hasegawa Y, Sugahara K, Horii N, Saito S, Nakao Y, Nanto T, Ono T, Domen K, Kishimoto H. **Change in Nutritional Status and Dysphagia after Resection of Head and Neck Cancer**. Nutrients 2021, 13(7).
20. Lopes S, Mesquita-Bastos J, Garcia C, Bertoquini S, Ribau V, Teixeira M, Ribeiro IP, Melo JB, Oliveira J, Figueiredo D, et al: **Effect of Exercise Training on Ambulatory Blood Pressure Among Patients With Resistant Hypertension**. JAMA Cardiology 2021.
21. Huang X, Li S-H, Tan Y-f, Yang H, Hu L, Li H-z. Application of oropharyngeal exercise combined with guided education in rehabilitation training of dysphagia in Patients with Alzheimer's disease (in Chinese). Modem Chnical Nursing. 2018;17(3):61–4.

Figures

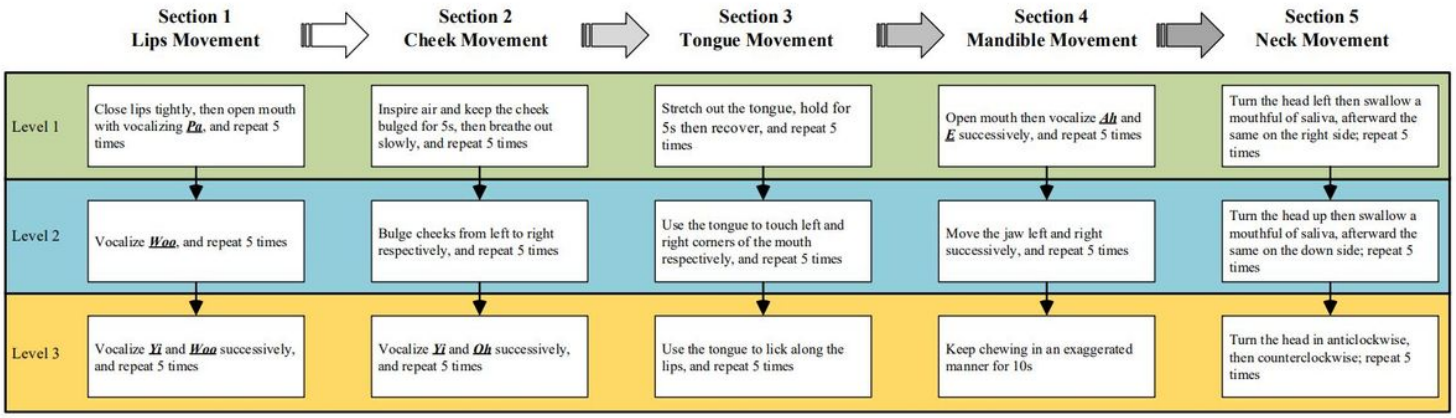

Figure 1

SST Flow Chart

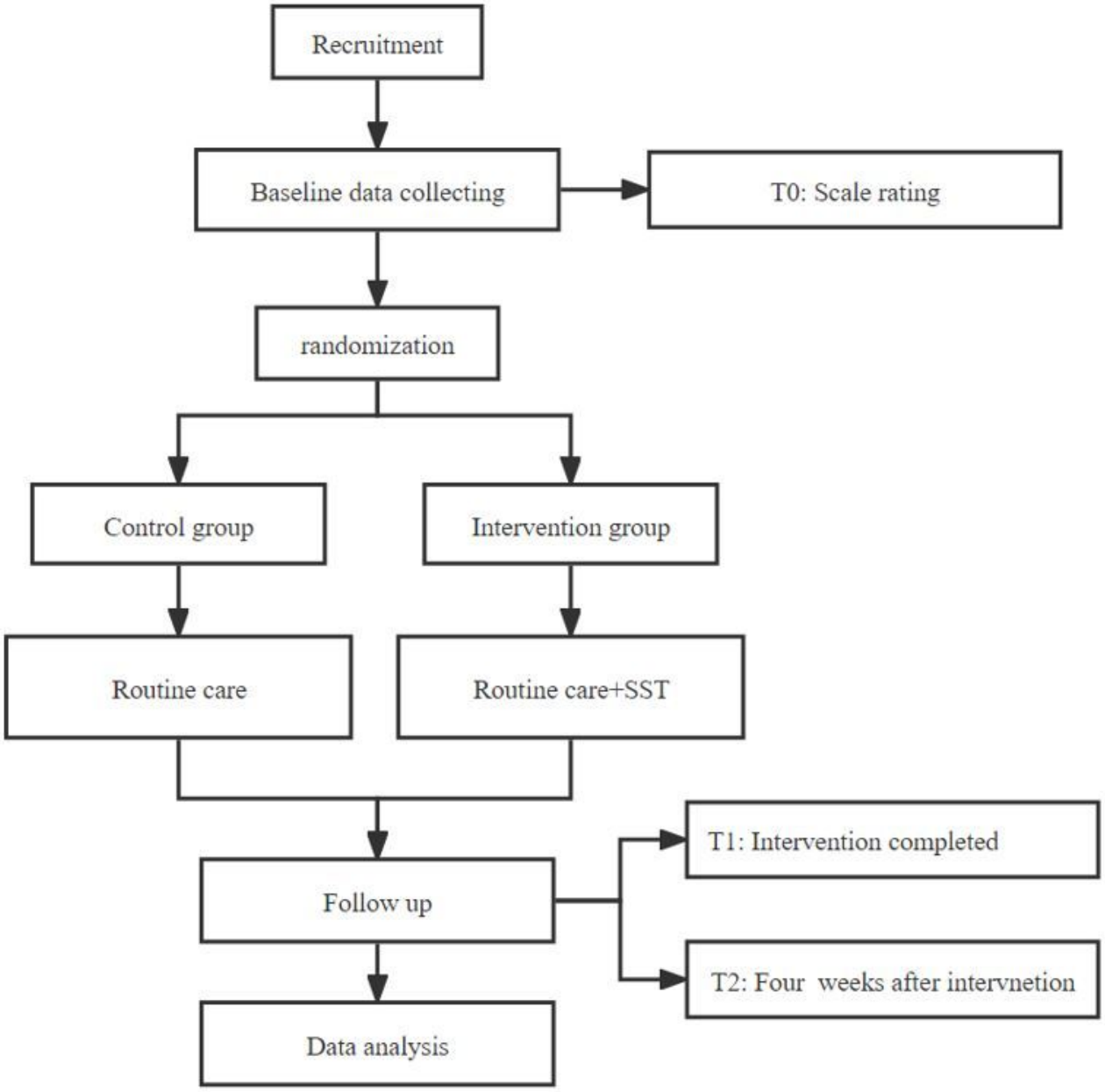

Figure 2

Protocol Flow Chart

Supplementary Files

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- 3.10SPIRITchecklist.docx