

Meta-analysis: The Effect of Muscle Strength Training on Walking Ability of Patients with Parkinson's Disease

Meng Zhaoli¹, Zhi Xiao¹, Li Beibei¹, Zheng Yanpei¹, Li Lin², Du Fei², Li Tong², Yan Zhi^{2, *},
Liang Zhanghua^{3, *}

¹School of Kinesiology and Promotion, Dalian University of Technology, Dalian, China

²Department of Neurology, Dalian Port Hospital, Dalian, China

³Department of Neurology, the First Affiliated Hospital of Dalian Medical University, Dalian, China

Email address:

mengzl@dlut.edu.cn (Meng Zhaoli), Xiao.zhi11@foxmail.com (Zhi Xiao), 839654641@qq.com (Li Beibei),
1570664704@qq.com (Zheng Yanpei), lilin13478754655@126.com (Li Lin), dufei198813@126.com (Du Fei),
hys907325@163.com (Li Tong), qjqiaojie@126.com (Yan Zhi), zhanhualiang@163.com (Liang Zhanghua)

*Corresponding author

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Abstract: *Objective:* This Meta-analysis was aimed to systematically studying the effects of muscle strength training on the walking ability like balance ability, mobility ability of Parkinson's disease patients and then provide useful theoretical reference to further researches on exercise treatments on Parkinson's disease by retrieving and collecting articles about muscle strength training. *Methods* This literature review was finally determined on searching PubMed, Elsevier, Web of science, China Journal Full-text Database (CNKI), WanFang Data and other Chinese and foreign databases and combined with manual search. The limit of the search time was from the date when the literature was recorded to 2019. A comprehensive collection of randomly controlled trials of muscle strength training on the walking ability of Parkinson's patients was done. Researchers used the Cochrane risk assessment tool to evaluate the methodological quality of the selected articles, and the ReMan 5.3.5 software to statistically process the obtained data. *Results* A total of 13 RCTs and 627 samples were included in this study. Meta-analysis of BBS balance scale show that MD=4.67 (95%CI, I²=97%, P=0.52) between muscle strength training group and non-exercise intervention group; MD=-2.67 between muscle strength training group and exercise intervention control group (95%CI, I²=7%, P<0.00001); TUGT Meta-analysis show that MD=-1.06 (95%CI, I²=75%, P=0.10) between muscle strength training group and non-exercise intervention group; MD=0.09 (95%CI, I²=0%, P=0.31) between the muscle strength training group and the control group with exercise intervention; 10MWT Meta-analysis show MD=-0.28 (95%CI, I²=98%, P<0.29) between the muscle strength training group and the control group with exercise intervention; Stride length Meta-analysis show MD=-1.85 (95%CI, I²=68%, P=0.63) between the muscle strength training group and the control group without exercise intervention; MD=-1.75 (95%CI, I²=32%, P=0.56) between the muscle strength training group and the control group with exercise intervention; MD=-1.75 (95%CI, I²=32%, P=0.56). Meta-analysis of stride speed show MD=-0.02 (95%CI, I²=0%, P=0.46) between muscle strength training group and control group without exercise intervention; MD=-0.03 (95%CI, I²=35%, P=0.52) between the muscle strength training group and control group with exercise intervention. *Conclusion* Muscle strength training can significantly improve the balance ability, mobility, and walking ability of Parkinson's disease patients, but it has no significant benefits on improving stride length and walking speed.

Keywords: Strength Training, Parkinson's Disease, Walking Ability

1. Introduction

Parkinson's disease (PD) is a kind of neurodegenerative

disease, which is clinically manifested as akinesia (shortened step length, slower walking speed, often longer gait cycle time, increased step length variability and asymmetry), stiffness, tremors and unstable posture [1, 2]. According to statistics,

among people over the age of 50, the incidence rate is 70.7/100,000 [3], and the disability rate is high. It is reported that after 1 to 5 years of onset, the disability rate is 25%, and it could reach 66% after 5-9 years [4] and gradually became younger trend. Due to the impairment of the central and peripheral nerve control ability, the patient's muscle strength is reduced, which has a great correlation with the patient's risk of falling and slower walking speed [5] leads to a decrease in the patient's balance ability and gait disturbance. The fall rate and the mortality rate increases in the course of the disease has seriously affected the patient's mobility and quality of life.

In recent years, exercise intervention has been widely studied as a non-medical method for clinical auxiliary treatment of Parkinson's disease patients, which can improve patients' balance ability, gait disturbance, increase muscle strength, and prevent falls [6, 7]. Strength training is an intervention method to make effects on exercise through resisting resistance. Studies have proved that muscle strength training is an effective, safe and feasible exercise therapy that assists in the treatment of clinical features of patients with neurodegenerative diseases [8-10]. This research conducts a systematic review and meta-analysis of this type of related research to classify and analyze the clinical indicators of Parkinson's disease patients. According to the results, the study adopt subgroup analysis to summarize and evaluate the specific application of muscle training in clinical rehabilitation.

2. Materials and Methods

2.1. Literature Retrieval

PubMed, Elsevier, Web of science, China Journal Full-text Database (CNKI), WanFang Data and other Chinese and foreign databases with MeSH were retrieved. The keywords includes "parkinson disease", "parkinson's disease", "Strength training", "resistance training", etc. A total of 2490 relevant documents were obtained, and 1119 were selected after screening and deduplication according to the research direction. After reading the abstract, 127 articles were included. 95 articles variables did not meet the inclusion criteria, and the remaining 32 articles were read. The outcome indicators of the 19 articles could not be obtained in the form of mean \pm standard deviation ($\bar{X} \pm S$), and finally 13 articles were included in this meta-analysis.

2.2. Inclusion Criteria

The quality of the included research literature directly affects the reliability and validity of the meta-analysis results. In order to get qualified studies, there must be strict screening criteria: (1) The study of the influence of muscle strength training on the gait of patients with Parkinson's disease must be randomized clinical trials (RCT); (2) Patients who have been diagnosed with Parkinson's disease according to the British Brain Bank Parkinson's disease diagnostic criteria [10]; (3) The training method of the experimental group is strength training (including resistance training) while the control group received other exercise intervention therapy or blank control;

(4) The variables include BBS/Berg balance scale, stride length, walking speed, time up to go test (TUGT), and 10-meter walk test (10 meters walking test, 10MWT); (5) Electronic full text is available.

2.3. Data Information Extraction

The content of data extraction includes: (1) Basic information of the literature, such as author, year of publication; (2) Trial design includes randomization, control, blinding, etc.; (3) General information of the research objects obtain age, number of research objects, intervention methods, total intervention time, outcome indicators, etc. If the included RCT in the literature involves multiple grouping studies, extract the experimental group and the control group that are consistent with the purpose of this research. The data is showed in the form of mean \pm standard deviation ($\bar{X} \pm S$).

2.4. Statistical Analysis

RevMan 5.3.3 statistical software was used for bias assessment, heterogeneity test, data merging, and drawing bias and forest maps. The data processed in this study was continuous data, and the 95% confidence interval of MD (Mean Differences) random effects model. (1) Heterogeneity test: Use I^2 to test heterogeneity, and I^2 test to judge the degree of heterogeneity. When $P > 0.1$ and $I^2 \leq 50\%$, the heterogeneity between the studies is considered to be small; when $P \leq 0.1$, $I^2 > 50\%$, the heterogeneity between the studies is considered to be greater. Low heterogeneity chooses fixed effects model (FEM) analysis, and high heterogeneity chooses random effect model (REM).

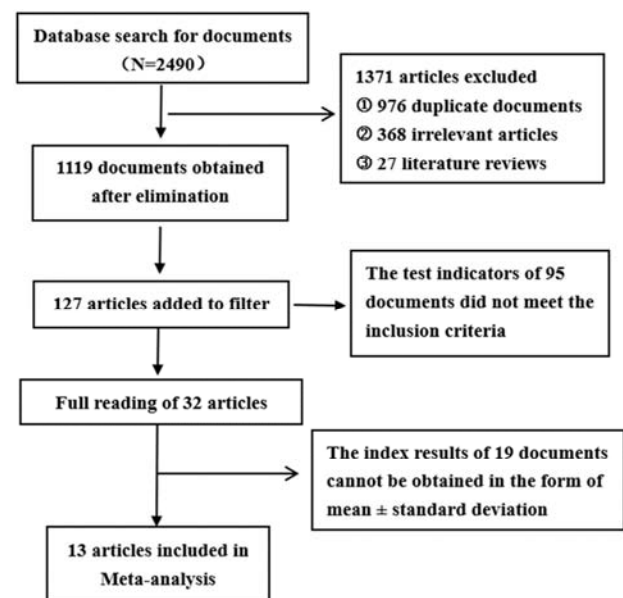


Figure 1. Screening Diagram of included literatures.

3. Results and Analysis

3.1. Discussion on Characteristics and Quality of Included Literature

A total of 13 [6, 11-22] articles on the influence of muscle

strength training on walking ability of Parkinson's disease were included in this study, and the research period was from 2013 to 2019. There were 5 Chinese literatures and 9 foreign literatures, all of them were randomized controlled trials. There were 6 studies for the experimental group to receive strength training, the control group only received drug therapy as a blank control. In 7 studies, the experimental group received strength training, the control group received another exercise interventions include balance training, aerobic training and treadmill training. A total of 627 patients aged from 40 to 77 years old were recruited in this study. The duration of intervention period was more than 8 weeks. (Table 1).

From the overall point of view of Table 1, there is bigger difference of age among subjects included in the literature (from 40 to 70 years old), which is mainly reflected in the research of Tang Jie et al. From the perspective of intervention duration, there were also some differences. Miriam et al. carried out a two-year follow-up survey on the strength and improved fitness program of patients with Parkinson's disease, which was significantly longer than other researches periods.

In addition, the loss rate of Parkinson's disease patients from recruitment to the end of the experiment was relatively high, which may lead to high risk of data integrity. These results may be the heterogeneous sources of data bias.

3.2. Assessment of Literature Bias

In this study, Cochrane Handbook (5.1.0 version) was used to comprehensively evaluate the literature quality [23]. Figure 2 shows the bias evaluation chart of the included literature, and Figure 3 shows the risk summary chart of the included literature. Bias evaluation mainly included the following aspects: (1) random allocation method. (2) allocation concealment. (3) implementation of blind method. (4) integrity of results data. (5) selective reporting of research results. (6) other biases. The evaluation of literature quality is based on the handbook standard: "unclear" or "low risk" or "high risk". It can be seen from Figure 2 and Figure 3 that there are some bias in the literature included in the analysis, but the overall quality of the literature was above medium.

Table 1. Basic characteristics of included literature.

Author	Year (y)	Number of subjects (E/C)	Age (E/C)	Intervention method	Exercise duration (w)	Variable
Tang Langjuan	2019	31/31	67.76±5.23/ 69.64±4.58	Resistance Training/ Conventional Treatment	12	BBS
Yu Mei	2015	37/34	63.5±8.2/ 65.2±7.4	Strengthen core strength training/ Comprehensive rehabilitation therapy	12	BBS Walking speed TUGT Stride
Tang Jie	2017	31/33	40-70	Strength training/Balance training	8	Walking speed TUGT Stride
Yang Yan	2018	18/18	58.95±4.66/ 58.01±4.62	Functional strength training/ Conventional rehabilitation training	8	BBS TUGT
Shen Jun (a)	2019	40/45	64.87±4.76/ 65.08±4.91	Resistance training/pramipexole	12	BBS
Shen Jun (b)	2019	40/45	64.87±4.76/ 65.08±4.91	Resistance training/Parkinson's operation	12	BBS
Xia Shai	2014	22/23	65.3±8.5/ 63.3±8.0	Strength training/Balance training	12	Walking speed Stride
Brian K Schilling	2010	9/9	61.3±8.6/ 57.0±7.1	Moderate amount of lower extremity resistance training with high load/ Conventional Treatment	8	TUGT
Miriam R. Raffsty (a)	2018	20/23	59.0 ±4.6/ 61.2±7.7	Progressive resistance training/Conventional Treatment	104	Walking speed Stride
Miriam R. Raffsty (b)	2018	20/18	59.0 ±4.6/ 58.6±5.6	Progressive resistance training/Improved fitness plan	104	Walking speed Stride
Marie DEMONCEA (a)	2017	15/15	67±10/ 63.3±6	Strength training/Conventional Treatment	12	Walking speed Stride
Marie DEMONCEA (b)	2017	15/16	67±10/ 65±8	Strength training/Aerobic training	12	Walking speed Stride
Alessandro Caivalho (a)	2015	8/9	64.1±9.9/ 62.1±11.7	Strength training/Physical therapy	12	BBS 10MWT
Alessandro Carvalho (b)	2015	8/5	64.1±9.9/ 64.8±11.9	Strength training/Aerobic training	12	BBS 10MWT
Lisa M. Shulman (a)	2013	22/23	65.3±11.3/ 66.1±9.7	Stretch resistance training/ High intensity treadmill training	12	10MWT
Lisa M. Shulman (b)	2013	22/22	65.3±11.3/ 65.8±11.5	Stretch resistance training/ Low intensity treadmill training	12	10MWT
Chris J. Hass	2012	9/9	64±7/67±8	Progressive resistance training/Conventional Treatment	10	Stride
MAIHEUS BARBALHO	2019	7/8	77.14±1.08/ 77.63±0.60	Progressive resistance training/Conventional Treatment	12	10MWT

E/R: E=experiment, C=control

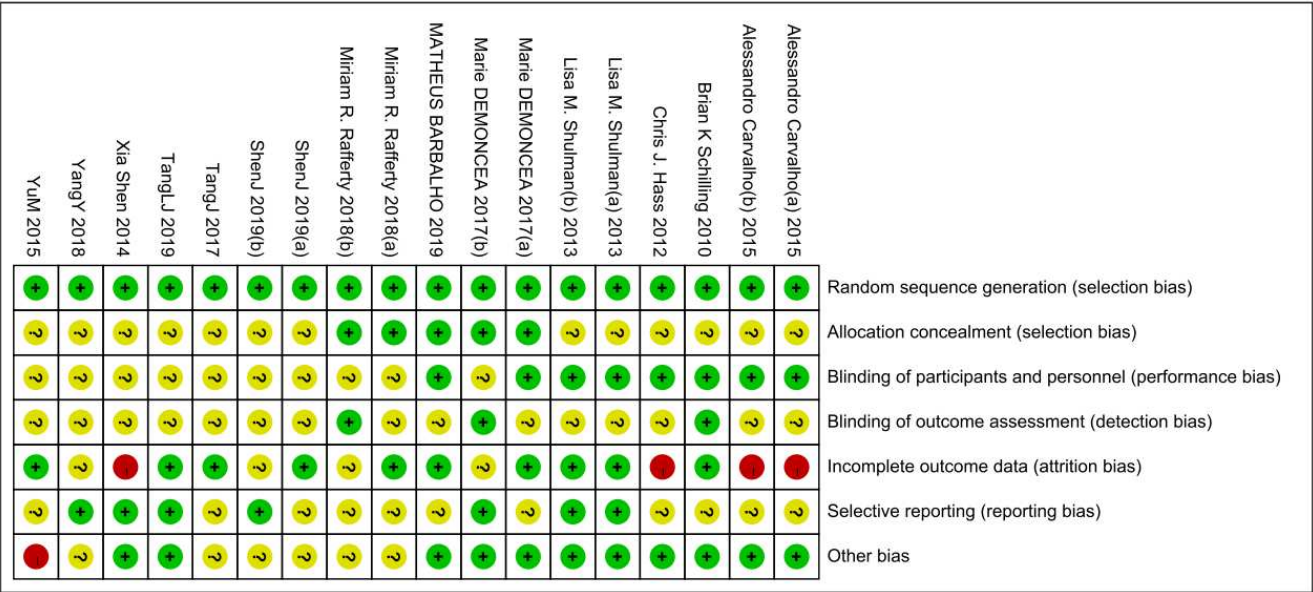


Figure 2. Schematic diagram of bias risk evaluation.

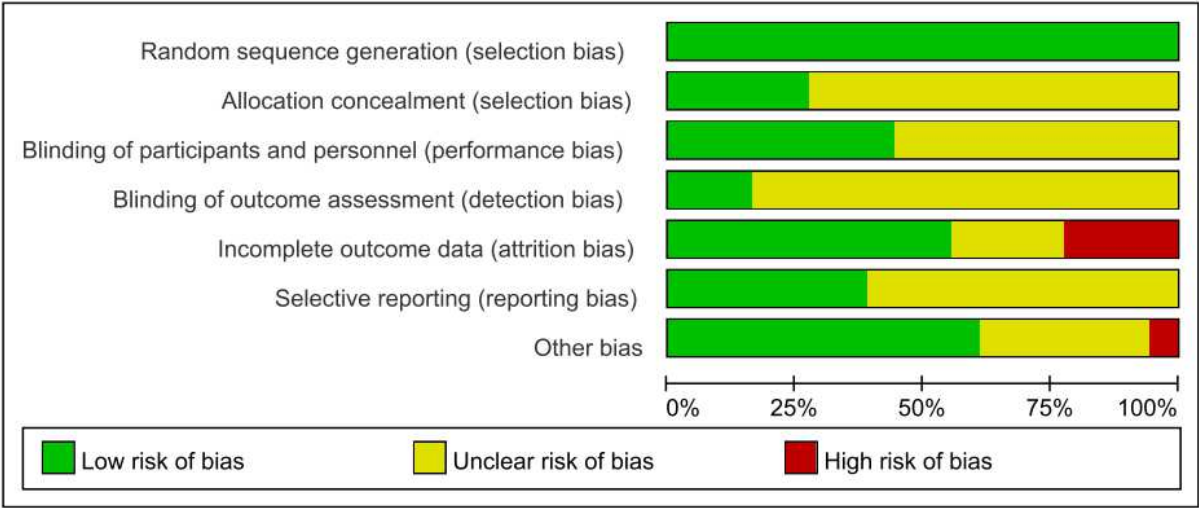


Figure 3. The ratio of risk of bias.

3.3. Subgroup Analysis

According to the difference of research design, the literature is divided into two categories. (1) Strength training group (experimental group) versus non exercise intervention group (control group); (2) strength training group (experimental group) versus exercise intervention group (control group). The influence of strength training on balance ability and motor ability of patients with Parkinson's disease was discussed by subgroup analysis.

3.4. Main Results of Meta-analysis

3.4.1. Meta-analysis of BBS Balance Scale

As shown in the meta-analysis of BBS balance scale in figure 4 and figure 5, the combined data analysis of experimental group and non exercise intervention group

showed heterogeneity ($I^2=99.64$, $P<0.00001$, $I^2=97\%$), 95% total effect confidence interval 1.67 [-3.41, 6.75], $P=0.52$. And the combined data analysis of the experimental group and the control group with exercise intervention showed heterogeneity ($I^2=2.16$, $P=0.34$, $I^2=7\%$), 95% total effect confidence interval -2.67 [-3.68, -1.65], $P<0.00001$).

3.4.2. TUGT Meta-analysis

Figure 6, the combined data analysis of the experimental group and the non exercise intervention group showed heterogeneity ($I^2=12.10$, $P=0.007$, $I^2=75\%$), 95% total effect confidence interval -1.06 [-2.32, 0.20], $P=0.10$. And the combined data analysis of the experimental group and the control group with exercise intervention showed heterogeneity ($I^2=0.19$, $P=0.67$, $I^2=0\%$), 95% total effect confidence interval 0.09 [-0.08, 0.27], $P=0.31$.

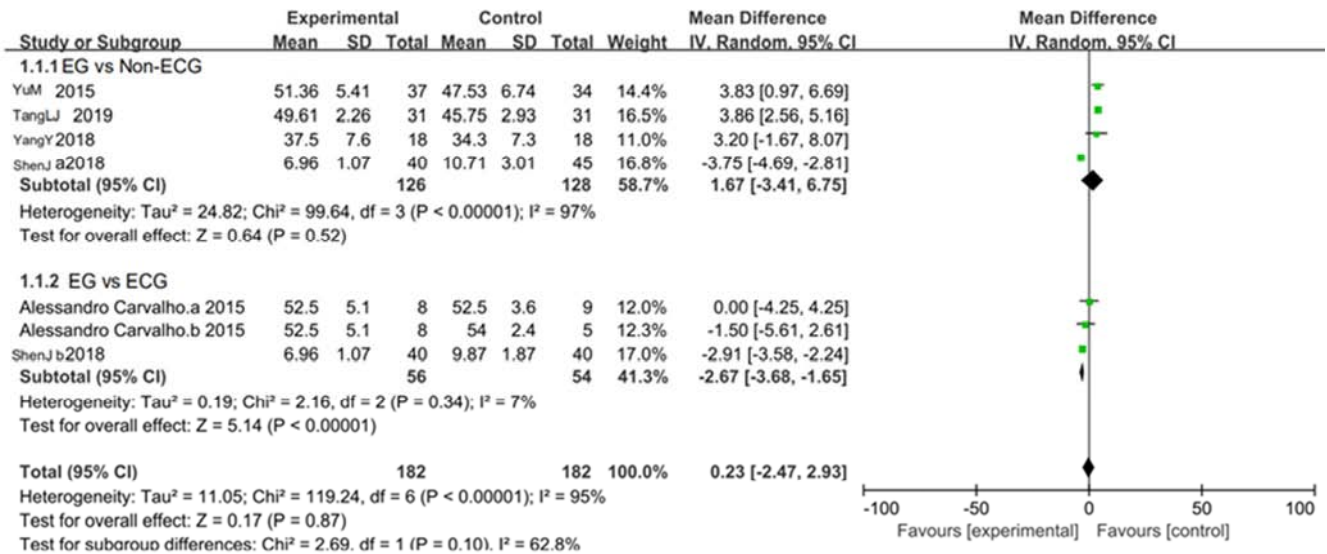


Figure 4. Meta-analysis forest diagram of BBS balance scale (1).

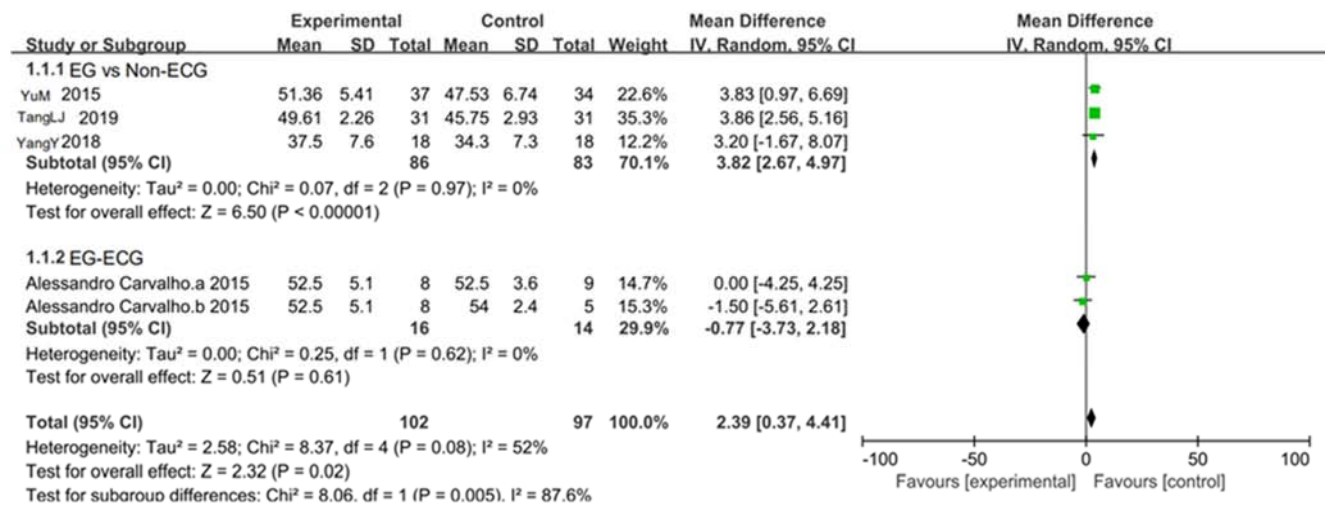


Figure 5. Meta-analysis forest diagram of BBS balance scale (2).

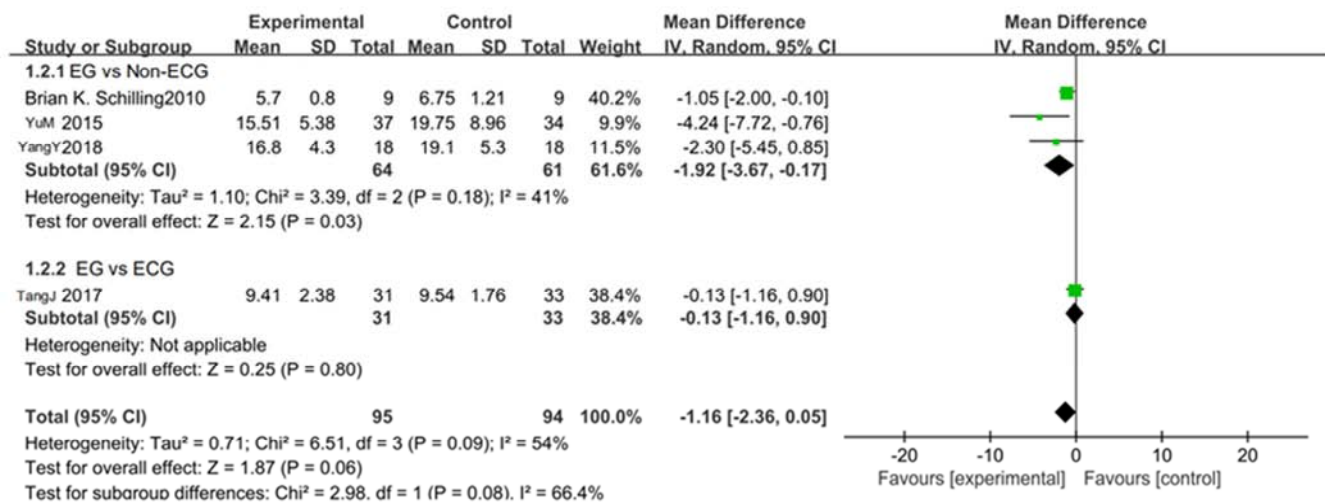


Figure 6. TUGT Meta-analysis forest map.

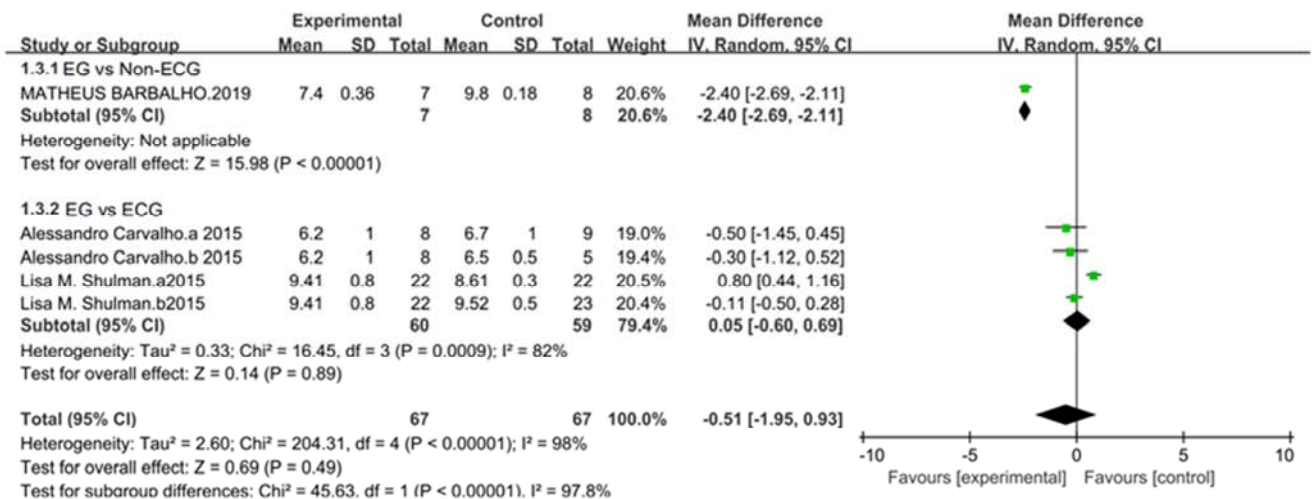


Figure 7. 10MWT Meta-analysis forest map.

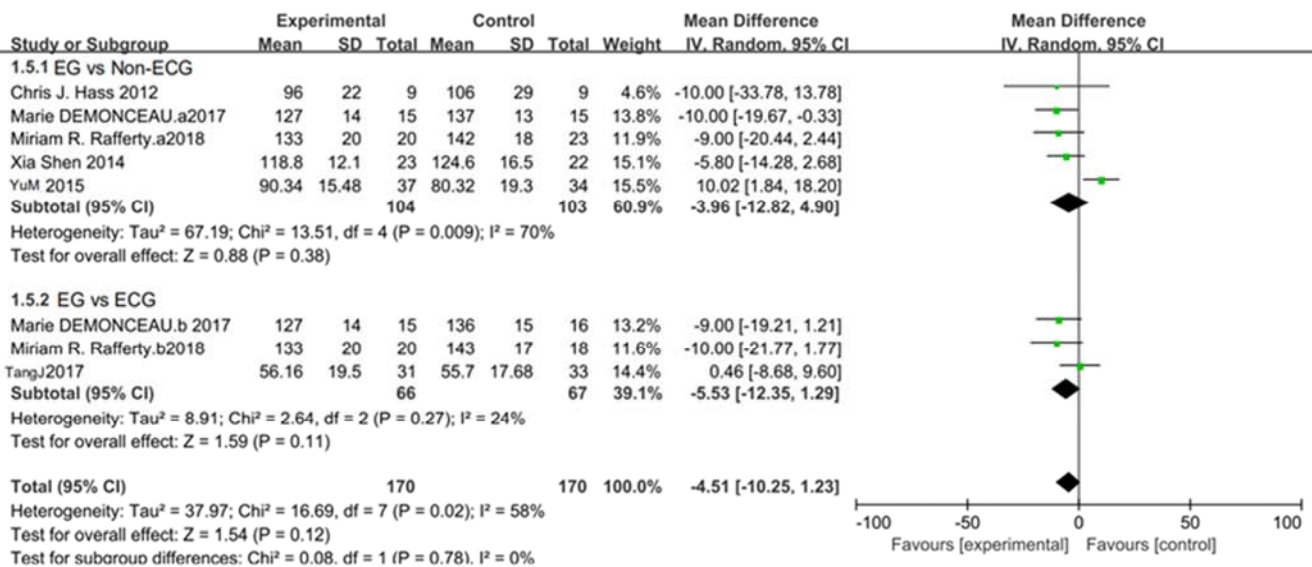


Figure 8. Stride Meta-analysis Forest Map.

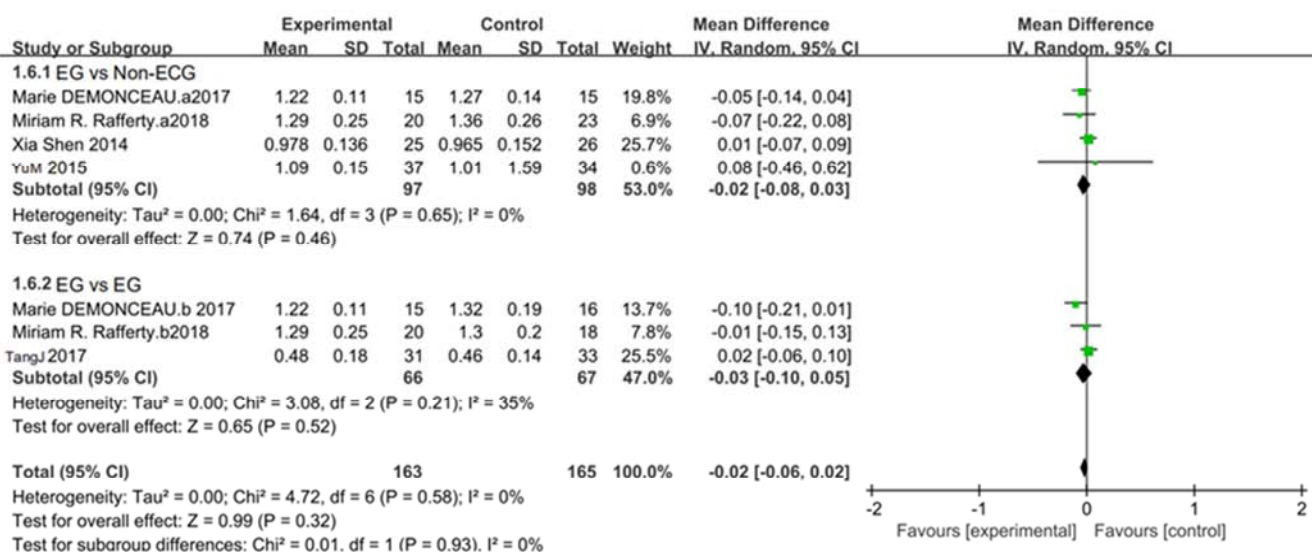


Figure 9. Meta-analysis forest diagram of pace.

3.4.3. 10MWT Meta-analysis

As shown in Figure 7, the combined data analysis of the experimental group and the control group with exercise intervention showed heterogeneity ($I^2=138.96$, $P<0.00001$, $I^2=98\%$), 95% total effect confidence interval -0.82 $[-2.36, -0.71]$, $P<0.00001$.

3.4.4. Meta-analysis of Stride Length

In Figure 8, the combined data analysis of the experimental group and the control group with non exercise intervention showed heterogeneity ($I^2=12.61$, $P=0.01$, $I^2=68\%$), 95% total effect confidence interval -1.85 $[-9.27, 5.57]$, $P=0.63$. And the combined data analysis of the experimental group and the control group with exercise intervention showed heterogeneity ($I^2=2.93$, $P=0.23$, $I^2=32\%$), 95% total effect of confidence interval -1.75 $[-7.59, 4.10]$, $P=0.56$.

3.4.5. Meta-analysis of Walking Speed

As shown in Figure 9, the combined data analysis of the experimental group and the control group with non exercise intervention showed heterogeneity ($I^2=1.64$, $P=0.65$, $I^2=0\%$), 95% total effect confidence interval -0.02 $[-0.08, 0.03]$, $P=0.46$. And the combined data analysis of the experimental group and the control group with exercise intervention showed heterogeneity ($I^2=3.08$, $P=0.21$, $I^2=35\%$), 95% total effect confidence interval -0.03 $[-0.10, 0.05]$, $P=0.52$.

4. Discussion

Weakened muscle strength leads to slower walking speed, weaker postural control ability and mobility in Parkinson's disease patients [24-25], which is also one of the independent factors leading to falls among the elderly people [26]. Amyotrophy caused by dopamine levels decline in Parkinson's disease leads to less stimulation through the basal ganglion-muscle or nerve-muscle pathway. In addition, most patients with Parkinson's disease are living a sedentary lifestyle and that is also a major cause of Amyotrophy. Muscle strength training can increase the nerve driving force by generating stimulation, as a result of recruiting more motor units (increase of motor muscle fibers) in order to increase muscle strength so that preventing fall [27] when patients are prone to. The results of this study showed that, compared with the control group without exercise intervention, muscle strength training had no effect on the balance ability of PD patients. After the inclusion [19] was eliminated according to the method of exclusion literature one by one, the result was positive ($P<0.00001$, Figure 5). Compared with exercise intervention in the control group, there was no significant improvement through strength training than aerobic training and Parkinson's exercise training on the BBS score ($P=0.61$, figure 4), the reasons for this result may be participants selected in the study of [19] had lower BBS score compared to other researchers at baseline. So a conclusion can illustrate that the study may be the heterogeneous sources of BBS subgroup analysis. TUGT and 10MWT respectively reflect the mobility of patients (the ability to perform other activities

from sitting position to standing position and then to walking) and mobility. These two tests are widely used as the effectiveness and sensitivity indexes to evaluate patients' ability of activities of daily life [28-31]. The results of TUGT and 10MWT Meta-analysis showed that muscle strength training improved the mobility and walking ability of PD patients and meanwhile reduced the risk of falls of them to a certain extent, which were consistent with the results of Leland E. Dibble et al [32]. As for stride length, walking speed subgroup meta-analysis, muscle strength exercise group compared with control group without intervention and the control group with intervention, these two numbers of values did not change significantly before and after the intervention. According to N. E. Allen's mentioned in the study, the proper strength training can improve the muscle strength of patients with PD, there are also researchers believe that strength training is a kind of muscle power training that is the way to train the ability of fast muscle strength output. Lower muscle power output is also the reason why the elderly walk slow when they are aged.

Motor unit is mainly composed of two different kinds of motor units, type I and type II. The contraction speed of Type I motor unit is slower but not easy to fatigue, while type II has reverse characters compared type I, Type I units are raised first when muscles start to work and then type II units would be recruited if movements need more muscles to stimulate in order to quickly produce stronger power to complete the muscle activity. Strength training is mainly to increase muscle strength, and muscle output power training is to improve the ability to produce more strength quickly. However, the effectiveness of muscle strength training increase the ability of PD patients' movement speed has not been confirmed [26]. Therefore the influence of muscle strength training on walking speed and stride length needs to be further clarified.

5. Conclusion

In summary, muscle strength training significantly improved the balance ability and mobility of PD patients, but it is not seen that obvious improvements on stride length and walking speed. The duration of practice was shorter in some articles and the true effect on rehabilitation in patients may not have been fully manifested.

In this Meta-analysis, there are also some differences in the number of subjects, intervention methods and intervention duration among the included articles. Thus more high-quality literatures should be included for classification study, so as to further verify the impact of muscle strength training on walking ability of PD patients.

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