Are Aerobic Programs Similar in Design to Cardiac Rehabilitation Beneficial for Survivors of Stroke? A Systematic Review and Meta-Analysis

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Background—Survivors of stroke face movement disability and increased cardiovascular disease and stroke risk. Treatment includes rehabilitation focused on functional movement with less emphasis on aerobic capacity. After rehabilitation, survivors of stroke must self-manage activity with limited appropriate community programs. Lack of structured activity contributes to sedentary behavior. The objective of this systematic review and meta-analysis is to review aerobic programs for stroke survivors similar in activity and dosage to cardiac rehabilitation programs to determine their efficacy for improving aerobic and walking capacity.

Methods and Results—Preferred Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used to review 5 databases. Group interventions for survivors of stroke with a primary aerobic component and dosage from 18 to 36 visits over 8 to 18 weeks (matching cardiac rehabilitation requirements in the United States) were included. The 6-minute walk test, maximal oxygen consumption (VO2) peak, and walking speed were included as measures of aerobic capacity. Summary effect sizes and outcome measure mean differences were calculated for preintervention to postintervention, and summary effect sizes were calculated for preintervention to follow-up. Activity type and initial 6-minute walk test moderator analyses were performed. Nineteen studies with 23 eligible groups were selected. Survivors of stroke improved their composite aerobic capacity with an effect size of 0.38 (95% CI, 0.27–0.49). Studies including 6-minute walk test demonstrated a pooled difference in means of 53.3 m (95% CI, 36.8–69.8 m). Follow-up data were inconclusive.

Conclusions—Survivors of stroke benefit from aerobic programs with similar dosing to cardiac rehabilitation in the United States. The potential integration into existing programs could expand the community exercise options. (J Am Heart Assoc. 2019;8:e012761. DOI: 10.1161/JAHA.119.012761.)

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Clinical Perspective

What Is New?

- Reviewing efficacy of aerobic programs for survivors of stroke similar in activity and dosing to cardiac rehabilitation in the United States provides a prerequisite knowledge base for considering application of cardiac rehabilitation after stroke.
- Results of the systematic review and meta-analysis indicate aerobic programs similar in activity and dosing to cardiac rehabilitation programs in the United States are effective at increasing aerobic capacity for survivors of stroke regardless of mode of exercise, functional mobility, or time since stroke.

What Are the Clinical Implications?

- Providing cardiac rehabilitation for survivors of stroke may positively impact health status and mobility without creating new programs; further research is warranted.

Methods

All data and materials have been made publicly available at Open Science Framework.28

Search Strategy


Inclusion and Exclusion Criteria

Inclusion of studies was further evaluated by the presence of the following characteristics to obtain similarity to US CR program requirements16,17:

1. A population of adult survivors of stroke.
2. A study design that included pretesting and posttesting for an intervention for at least one group.
3. An intervention type that was group based and included a primary aerobic exercise component with the optional addition of resistance exercise, stretching, or educational sessions.
4. An intervention dosage of 18 to 36 total visits over 8 to 18 weeks.
5. Outcome measures that included at least one measure of aerobic capacity: 6-minute walk test (6MWT), other time-limited walk tests, walking speed, or VO2 peak.

Presence of the following excluded the study from the current review:

- Presence of the following excluded the study from the current review:
1. Studies that included physical therapy or other interventions in addition to aerobic exercise other than resistance exercise, stretching, or educational sessions.
2. Studies that provided physical assistance to the participant through mechanical, technological, or physical assistance other than assistive devices or equipment setup.
3. Studies that were individual (nongroup) based.
4. Studies that used aquatic-based activities.

**Study Selection**

After completion of the database searches, references and abstracts were uploaded to the Covidence screening tool (http://www.covidence.org; Veritas Health Innovation, Australia) for review. Duplicates were removed. Initial title and abstract screening eliminated nonqualified studies based on inclusion and exclusion criteria by the primary author (E.R.). In addition, any relevant systematic review and meta-analysis reference lists were reviewed by the primary author during title and abstract screening. Studies that were not eliminated were reviewed further in full text against inclusion and exclusion criteria by 2 authors independently (E.R. and R.H.), with discrepancies resolved by discussion and consensus. Studies were included in the systematic review if they met all inclusion criteria, and studies were included in the meta-analysis if aerobic capacity data were available for preintervention and postintervention.

**Quality Assessment**

Quality assessment was completed by the lead author (E.R.) using the Physiotherapy Evidence Database quality (PEDro) scale for clinical trials. PEDro is an accepted method for reviewing methodological rehabilitation studies independently and as part of systematic reviews, and it has been recommended over other scales for evaluation of stroke rehabilitation literature. PEDro assesses 11 criteria, awarding 1 point for each criterion that is clearly satisfied and 0 points when there is the possibility that the criterion is unsatisfied.

**Data Extraction**

Descriptive data extracted from studies included author, year of publication, study country, study setting, interventionalist, activities in intervention, total visits, frequency, duration, and participant demographic information. Outcome measure data were extracted from studies for comparison of pretest and posttest means and SDs. Follow-up data, where available, were also extracted. Data conversions were made for 2 studies to allow for use in the meta-analysis. The Severinsen et al (2014) study was standardized from median to means and SDs using methods described by Hozo et al. In the 2006 study by Olney et al, 6MWT was presented in m/s and was converted to m. The authors of the study by Awad et al (2016) were contacted to obtain 6MWT data that were not presented in the publication.

**Data Analysis**

Comprehensive Analysis Software (Version 3; Biostat) was used to perform all statistical calculations. A random-effects model was used for all comparisons as a conservative approach because of clinical heterogeneity of studies and multiple studies with small sample sizes. The I² statistic was calculated to determine relative variance between studies.

**Calculating Effect Sizes and Mean Differences**

Summary effect sizes (Hedges g) were calculated for all the studies preintervention to postintervention and preintervention to follow-up using a composite mean of aerobic capacity outcome measures: 6MWT, VO₂ peak, maximum walking speed (MWS), and self-selected walking speed (SSWS). In addition, pooled mean differences for each individual outcome measure were calculated. 6MWT, VO₂ peak, MWS, and SSWS are all accepted measures of aerobic capacity and often correlate with one another.

**Moderator Analysis**

Evaluation of the summary effect sizes grouped by activity type (walking, cycling, or mixed aerobic activity) was a prespecified moderator analysis to determine if aerobic activity type impacted results. In addition, a post hoc moderator analysis of the 6MWT mean differences was performed by grouping those studies with a mean initial 6MWT value of ≥288 m (unlimited community ambulator) and <288 m (limited community ambulator) to examine differences in responses to aerobic activity between those with differing initial walking capacity.

**Sensitivity Analysis and Publication Bias**

Sensitivity analysis was performed using a one study removed strategy by removing the study group with the largest and smallest effect size in preintervention to postintervention and preintervention to follow-up to determine impact on summary effect size.

Publication bias was evaluated using funnel plots of summary effect and classic fail-safe N statistic for summary effect size for preintervention to postintervention and for preintervention to follow-up.
Results

Description of Studies

The review identified 19 qualified studies, some with multiple eligible treatment groups, for a total of 23 qualified treatment groups, including 485 participants with treatment group mean ages between 54 (SD, 8.6) and 71 (SD, 7) years. PRISMA process results are presented in Figure 1. Details on the study and treatment group characteristics are provided in Table S1. Only 4 of the 19 qualified studies were performed in the United States; the remaining were performed in Australia (n=2), Canada (n=2), Europe (n=8), Israel (n=1), Jamaica (n=1), and Taiwan (n=1). Frequency, duration, and activity type varied. Frequency of sessions was either 2 or 3 times per week. Session duration varied from 30 to 90 minutes, with the longer sessions including activities in addition to the primary aerobic exercise. Walking (treadmill or over ground) was the most common aerobic exercise performed (47%), followed by stationary cycling (21%), mixed-mode aerobic exercise (21%), and recumbent stepping (11%). Aerobic activity was performed at various intensities and was either continuous (ie, 1 bout of 30 minutes) or interval (ie, 3 bouts of 10 minutes). Additional activity was included in some studies and was composed of resistance training (21%), flexibility interventions (5%), and education (5%). Participant time since stroke varied (treatment group means from 0.06 [SD, 0.06] to 9.15 [SD, 12.72] years), with 1 study in the acute phase (≤30 days poststroke), 4 studies in the subacute phase (>30 days to <6 months poststroke), 12 studies* in the chronic phase (≥6 months poststroke), and 2 studies not reporting time since stroke. The functional level of participants at the start of the studies varied, with all except one study requiring some level of independent ambulation (with or without an assistive device); the exception

*References 33, 35, 36, 43, 44, 46, 47, 49–51, 54, 58.
was a cycling study, the study by Vanroy et al (2017),\textsuperscript{55} which required pedaling at 50 revolutions per minute.

**Quality Assessment**

Results of the PEDro assessment are presented in Table S2. Study quality varied because of the different study designs, ranging from single-group convenience samples to randomized control trials with control groups and assessor blinding. PEDro scores ranged from 3 to 9, with a median of 7 of a possible 11. Existing stroke rehabilitation literature has a median score of 6.\textsuperscript{39} Because concealment of therapists and participants is difficult in exercise intervention trials, these criteria are often unmet in rehabilitation studies.\textsuperscript{31,59}

**Preintervention to Postintervention Results**

Changes in aerobic capacity for preintervention-postintervention are presented in Figure 2. The summary effect size of the 23 treatment groups for improving aerobic capacity preintervention-postintervention was 0.38 (95% CI, 0.27–0.49), indicating a small positive effect.\textsuperscript{60} The \( I^2 \) statistic was 24.8%, indicating low variance in effect size between studies.

Individual outcome measure results also indicated small positive effects for each measure. The 6MWT results from 20 treatment groups had a summary effect size of 0.41 (95% CI, 0.25–0.58) and a pooled difference in means of 53.3 m (95% CI, 36.8–69.8 m). MWS (7 treatment groups) and SSWS (10 treatment groups) had similar improvements. MWS had a summary effect size of 0.28 (95% CI, 0.15–0.40) and a pooled difference in means of 0.12 m/s (95% CI, 0.07–0.18 m/s), whereas SSWS had a summary effect size of 0.29 (95% CI, 0.15–0.43) and a pooled difference in means of 0.12 m/s (95% CI, 0.06–0.17 m/s). \( \text{VO}_2 \) peak summary effect size was 0.38 (95% CI, 0.17–0.60), and the pooled difference in means was 2.08 mL/kg per minute (95% CI, 1.18–2.98 mL/kg per minute).

**Preintervention to Follow-Up Results**

When comparing the summary effect size for preintervention to follow-up, fewer data were available; 7 treatment groups within 6 studies resulted in a summary effect size of 0.22 (95% CI, −0.07 to 0.50), although this was not statistically significant. The forest plot is provided in Figure 3.

**Moderator Results**

**Activity Type**

Summary effects, moderated by activity type, resulted in a summary effect size 0.24 (95% CI, 0.10–0.57) for cycling or recumbent stepping (7 treatment groups), 0.37 (95% CI, 0.23–0.52) for walking (12 treatment groups), and 0.61 (95% CI, 0.44–0.78) for treadmill or stepping (4 treatment groups), indicating a small, moderate, and large effect size, respectively.
0.26–0.96) for mixed aerobic activity (4 treatment groups). The forest plot is displayed in Figure 4.

**Initial Performance on the 6MWT**

The 6MWT mean differences were divided into sets based on initial 6MWT of either <288 m (limited community ambulators) or ≥288 m (unlimited community ambulators). Participants with an initial 6MWT of <288 m demonstrated a mean gain of 37.5 m (95% CI, 25.7–47.3 m), whereas participants with an initial 6MWT of ≥288 m demonstrated a mean gain of 81.4 m (95% CI, 58.2–104.6 m). Results are presented in the forest plot in Figure 5.

### Sensitivity and Publication Bias Results

#### Preintervention to Postintervention

One study removed sensitivity analysis revealed the lowest overall resulting effect size of 0.35 (95% CI, 0.25–0.44) if the Sandberg et al (2016) group was removed. Removing the Lee et al (2008) treatment group (cycle only) resulted in the highest effect size of 0.39 (95% CI, 0.27–0.49). Neither of these changes significantly affected the results.

The funnel plot for review of publication bias for the preintervention-postintervention effects is slightly asymmetrical.
suggesting some bias toward smaller effect sizes. The funnel plot is presented in Figure 6. The classic fail-safe N is 364, which can be interpreted as needing 364 more studies to change the direction of the effect size.42 The funnel plot combined with the classic fail-safe N statistic suggest no impact of publication bias.

Preintervention to Follow-Up

The preintervention to follow-up results were not statistically significant. However, when removing the Severinsen et al (2014)33 treatment group (cycle), which had the only negative effect size, the summary effect size of 0.30 (95% CI, 0.08–0.53) became statistically significant. The reverse is also true: if the largest positive effect size treatment group, Awad et al (2016–1)36 (fast walking), is removed, the pooled effect became smaller and remains not statistically significant at 0.13 (95% CI, –0.12 to 0.38). Classic fail-safe N suggested only 5 more studies would be required to change the direction of effect. This result indicated publication bias and sensitivity to one study; therefore, preintervention to follow-up results are cautiously interpreted.

Discussion

Aerobic exercise programs that match the dosage of US CR programs improve aerobic capacity for survivors of stroke, regardless of the type of aerobic activity performed. Additional analysis by activity type suggests that walking (effect size (ES)=0.37) or mixed aerobic activity (ES=0.61) may be more beneficial to aerobic capacity than cycling alone (ES=0.24). Individual treatment groups with large overall aerobic capacity effect sizes, Hedges g >0.838 (Awad et al [2016–1],36 Sandberg et al [2016],52 and Yang et al [2007]55), were either mixed activity or treadmill walking; and all included participants with high levels of function (participants with minor stroke or the study had sizeable walking requirements). These results are clinically important because they indicate that applying walking or mixed aerobic exercise for those with mild impairments may maximize gains in aerobic capacity.

The 6MWT is a reliable measure of walking capacity and community ambulation for survivors of stroke.61 Survivors of stroke obtain clinically meaningful improvements in 6MWT distance after participation in aerobic exercise programs regardless of mode of exercise, functional level, or time since...
stroke. Despite different baseline 6MWT distances (capacities), all groups experienced improvements in aerobic capacity postintervention, as evident by the pooled difference in means of 37.5 m for those with an initial 6MWT <288 m and 81.4 m for those with an initial 6MWT ≥288 m. Although the quantity of improvement in the 6MWT was greater in treatment groups with higher initial performance, all exceeded the minimal clinically important difference of 34.4 m for survivors of stroke. The substantially higher result (81.4 m) for those with a higher initial 6MWT indicates that those with the mildest impairments may make the most overall gains. However, impact on community ambulation may be more pronounced for participants with a lower initial 6MWT. A study by Fulk et al demonstrated that the 6MWT has strong predictive value for determining whether survivors of stroke are home ambulators (<205 m), limited community ambulators (≥205 and <288 m), or unlimited community ambulators (≥288 m). Limited community ambulation consists of walking outside the house to at least the mailbox or car, and as far as down the block. Unlimited community ambulation includes the ability to navigate uneven terrain, shopping, and public venues. Each treatment group with baseline 6MWT distances of <288 m demonstrated an overall mean of 250.6 m in initial 6MWT distance, with a range of 225 to 273.5 m, corresponding to the limited community ambulator category; many (58%) transitioned to the unlimited community ambulator category after the intervention. For survivors of stroke, additional capacity may lead to improved community participation and independence. This noteworthy finding supports the benefits of aerobic exercise interventions for survivors of stroke regardless of initial performance on the 6MWT.

Walking speed mirrored 6MWT results, with all studies reporting initial MWS in the limited (0.4–0.8 m/s) or unlimited (>0.8 m/s) community ambulation category. In addition, initial SSWS were primarily at community ambulation speeds, except for one study, Vanroy et al (2017), which had an initial SSWS of 0.35 m/s, indicating household ambulation status. Although walking speed improved from preintervention to postintervention, the pooled mean differences of 0.12 m/s in both MWS and SSWS failed to meet the minimal detectable change in survivors of stroke (0.18 m/s for SSWS and 0.13 m/s for MWS). The treatment group in the study by Vanroy et al (2017) improved SSWS to 0.53 m/s and, therefore, all SSWS postintervention treatment group values had community ambulation status. In addition, all postintervention MWS treatment group values were in the unlimited community ambulation status.

VO₂ peak values reflect peak oxygen consumption levels achieved during exercise as a reflection of aerobic capacity. Activities of daily living expend energy in the range of 10.5 to 17.5 mL/kg per minute. To function in higher-level activity above activities of daily living, more capacity is required. Treatment groups in this meta-analysis had initial VO₂ peak values ranging from 11.24 to 20.88 mL/kg per minute. Although a pooled change of 2.08 mL/kg per minute is not large, the gains in VO₂ peak could have a significant impact in activity tolerance and community engagement for survivors of stroke.

The results of follow-up data were inconclusive. Except for one study group (Severinsen et al [2014]) with clear reversal of improvements at the 12-month follow up, the remaining studies all maintained gains in the follow-up period. Although the pooled results, including the study by Severinsen et al, were not statistically significant, removing the study by Severinsen et al from the analysis resulted in a statistically significant summary effect size of 0.30 (95% CI, 0.08–0.53) with a maintenance of aerobic capacity gains. With few studies presenting follow-up data, and follow-up periods varying from 1 to 12 months, the true capacity in postintervention follow-up is unknown but results suggest gains can be maintained after intervention completion. Further studies including follow-up periods are required to determine if program gains are maintained over time and if program participation leads to independently managed exercise.

Existing CR programs are one programmatic opportunity for filling the gap in available aerobic activity programs for survivors of stroke. Our meta-analysis demonstrates that dosing and activity similar to CR programs benefits survivors of stroke across the recovery continuum (acute, subacute,
and chronic) by improving aerobic capacity. Using CR programs could provide a safe environment for survivors of stroke to exercise within existing healthcare infrastructure after formal rehabilitation ends. Survivors of stroke with mild impairments are potentially the simplest group to integrate into existing CR programs because of their similarities with traditional CR participants (few mobility impairments), and our results suggest that those with mild impairments can achieve the most gains in aerobic capacity. CR programs have been adopted in Canada with positive health results for those without mobility impairments in traditional CR and separately in CR-based programs specifically for survivors of stroke with mobility impairments. Additional research into the feasibility of US CR programs and other existing community-based aerobic programs for survivors of stroke could make a significant impact on their lives and health status without creation of entirely new programs.

Study Limitations

Because of the inclusion of multiple study designs, no control group comparisons were included as part of our review. Determining if intervention groups improve more than control groups could provide additional information on efficacy. Lack of available studies with follow-up data prevented full conclusions on the persistence of gains after intervention cessation. The narrow duration and frequency criteria limit the ability to determine if shorter duration or less frequent interventions could provide similar gains. Available studies are primarily in survivors of stroke with mild mobility impairments, preventing conclusions of aerobic capacity benefits for survivors of stroke with more severe limitations.

Conclusions

After formal rehabilitation, many survivors of stroke exhibit deficits in aerobic capacity, which impacts their health status and community participation. Group-based aerobic exercise can be an alternative to continued one-on-one care or discontinuing services completely. Survivors of stroke of varying time since stroke, age, sex, and initial aerobic capacity can benefit from structured group aerobic exercise. Those with fewer mobility impairments and better initial capacity achieve the largest gains in aerobic capacity. Integrating survivors of stroke into existing CR programs could address the deficit of available community programs appropriate for survivors of stroke and requires further research in the United States. More studies with follow-up periods after primary group intervention and evaluation of cost and healthcare use could provide insight on the importance of continued services and their economic impact.

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Disclosures

None.

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Regression


