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Rehabilitation Process and Outcome

Physical Activity and Exercise Engagement in Patients Diagnosed with Transient Ischemic Attack and Mild/Non-disabling Stroke: A Commentary on Current Perspectives

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ABSTRACT: Individuals diagnosed with a transient ischemic attack (TIA) or mild/non-disabling stroke are at high risk of cardiovascular or recurrent cerebrovascular (stroke, TIA) events. Pharmacological intervention (ie anti-platelet and anti-coagulant medication) is considered the cornerstone of secondary prevention care for this population group. However, recent research has explored the utility of non-pharmacological interventions (eg exercise, diet, education) in improving health outcomes and reducing the risk of secondary events in patients with TIA or mild/non-disabling stroke. This commentary discusses the efficacy of implementing exercise interventions as a part of the secondary care program for acute and non-acute TIA and stroke patients. Current perspectives and future research initiatives are also discussed.

KEY WORDS: TIA, stroke, exercise, rehabilitation, secondary prevention

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Introduction

Stroke is a leading cause of death worldwide, and is a prominent cause of chronic disability, causing significant physical and cognitive impairments.[1] Transient ischemic attack (TIA), however, is an ischemic brain attack with focal cerebral or retinal symptoms that last less than 24 hours, usually less than 1 hour,[2] and thus leave minimal impairment and no overt long-term effects.[3] Individuals classified with a non-disabling stroke have minor residual symptoms, which are managed by the same treatment paradigm as TIA. Individuals who experience a stroke or TIA are at heightened risk of subsequent vascular events, including myocardial infarction, stroke and secondary TIAs, and death.[4,5] In fact, approximately 15% of all strokes are heralded by a TIA.[6] As many patients who experience neurological symptoms consistent with a TIA fail to report to their healthcare provider, the true prevalence of TIA is likely to be higher than the statistics reported.[7]

Meta-analyses have demonstrated the short-term risk of stroke after TIA to be between 3–10% at 2 days and 9–17% at 90 days.[8,9] Moreover, individuals who experience recurrent strokes are at higher risk of fatality than those who have experienced a primary stroke, and for those who survive a second stroke, a higher proportion will experience long-term disability.[10] It has been reported that approximately 12% of patients will die within 12 months of initial TIA diagnosis.[11] Individuals who have had a TIA and survived the initial high-risk period have a 10-year stroke risk of 19%, and a combined 10-year stroke, myocardial infarction, or vascular death risk of 43% (4% per year).[12] Accordingly, TIAs provide serious short- and long-term cardiovascular and cerebrovascular health concerns. Importantly, modifiable vascular risk factors,

such as hypertension, tobacco use, hyperlipidemia, obesity, and physical inactivity, are powerful determinants of stroke and TIA risk.[1,13,14] As stroke is a leading cause of long-term disability in the United States,[1] a reduction in the prevalence of TIAs and stroke post-TIA may have substantial impact for hospital, rehabilitation (inpatient and outpatient), and medication costs. As such, there will be major public health benefits if interventions are developed that reduce the burden of recurrent stroke and disability following TIA.[15]

Secondary Prevention of Stroke and TIA

The secondary prevention of stroke and TIA is primarily governed by the prescription of anti-platelet and/or anti-coagulation agents, as well as blood pressure lowering and lipid lowering treatments.[16–22] However, several studies in patients with cerebrovascular disease have indicated that the strategies implemented for secondary prevention are often suboptimal.[23–25] For example, one meta-analysis has demonstrated that only 11% of adults from the United States who have a history of stroke or myocardial infarction have achieved control of their vascular risk factors,[26] while up to 52% of stroke patients are unable to name a single risk factor for stroke.[27] Non-pharmacological interventions, including exercise, dietary advice, lifestyle counseling, and patient education, may therefore have an important role to play in averting a secondary stroke or TIA.[16,28]

Evidence-based reviews and meta-analyses have explored the utility of non-pharmacological interventions for improving the vascular risk profile of people with, or at risk of, cardiovascular disease. Studies have demonstrated that dietary interventions elicit modest reductions in body weight,[29] total cholesterol, low-density lipoprotein (LDL) cholesterol, and systolic blood pressure (SBP) and diastolic blood pressure (DBP),[30] while other lifestyle interventions (exercise and diet, behavioral intervention, counseling, etc) may lead to sustained moderate weight loss and may be effective in the prevention and treatment of hypertension, diabetes, and dyslipidemia.[31] Exercise also exhibits significant health benefits by lowering blood pressure,[32,33] improving plasma lipoprotein status,[34,35] reducing body weight,[36] and enhancing glycaemic control.[37] Exercise-based cardiac rehabilitation, which often utilizes a multi-factorial strategy (exercise, dietary advice, lifestyle counseling), has been shown to improve each of the aforementioned risk factors (blood pressure, blood lipid profile, etc.) and reduce morbidity and mortality among patients with coronary artery disease.[38–41] Similarly, the burden of stroke can be substantially reduced following the implementation of targeted interventions that promote physical activity and a healthy diet, and reduce blood pressure and smoking.[42] A meta-analysis has shown that moderate and high levels of physical activity are associated with reduced risk of total, ischemic and hemorrhagic strokes.[43] More recently, a cross-sectional study has demonstrated that regular exercise is independently associated with lower all-cause mortality after stroke (HR 0.66, CI 0.44–0.99).[44] These findings are supported by a recent meta-epidemiological study of randomized controlled trials that compared the effectiveness of exercise versus drug interventions on mortality outcomes.[45] This study demonstrated that physical activity interventions were more effective than anti-coagulant and anti-platelet medications in reducing the risk of mortality post-stroke.[45] Despite these interesting trends, there is limited evidence concerning the importance of physical activity participation within secondary prevention care in patients diagnosed with stroke or TIA, as demonstrated in a recent Cochrane review.[28] When considering quality standards reported by the Royal College of Physicians, a retrospective cohort study highlighted that only 34% of TIA patients receive appropriate exercise advice following diagnosis.[21] Furthermore, previous research has shown that stroke patients engage in sedentary behaviors and little physical activity post-stroke,[44,46,47] and that there are very few structured physical activity interventions designed and aimed at reducing the risk of recurrent stroke.[48,49] In this regard, it has been suggested that 80% of recurrent vascular events could be prevented through a comprehensive multi-factorial lifestyle strategy, which incorporates an exercise component.[50,51] The purpose of this commentary is to consider research that has investigated the efficacy of implementing exercise for stroke and TIA populations.

Benefits of exercise for stroke and TIA populations. To date, very few studies have assessed the components that are traditionally used in cardiac rehabilitation program for patients diagnosed with stroke or TIA.[38,51–54] Those studies that have taken this line of interest have used either randomized controlled trials;[38,52,54] the gold-standard for clinical trials, or prospective cohort investigations.[51,53] The study by Lennon et al[38] was a seminal publication in this area of research.[28] This study evaluated the efficacy of a 10-week cardiac rehabilitation program in reducing cardiovascular disease (CVD) risk factors and improving health-related quality of life in non-acute ischemic stroke patients. This single-blinded, randomized controlled trial recruited 48 community-dwelling stroke patients to an outpatient rehabilitation program. Individuals were randomly assigned to an intervention (16 cycle ergometry sessions and 2 stress management classes) or to a control group (usual care). Significantly higher improvements in aerobic exercise capacity and a cardiac risk score (an algorithmic score based on age, resting blood pressure, smoking status, diabetic status, total cholesterol, and high-density lipoprotein [HDL] scores) were observed for individuals randomized to the outpatient rehabilitation program. Accordingly, the authors asserted that non-acute ischemic stroke patients can improve their cardiovascular fitness and reduce their CVD risk following regular participation in a cardiac rehabilitation program. This was more recently supported by Tang et al[55] who utilized a similar cardiac rehabilitation-type program for individuals with a mild to moderate stroke disability. The authors demonstrated that six months of regular exercise participation was effective in eliciting improvements in aerobic capacity.

Prior et al contributed to this area of interest by using a prospective cohort design whereby the feasibility and efficacy of a six-month outpatient cardiac rehabilitation program in improving secondary prevention care after TIA or mild/non-disabling stroke was examined.[51] In their study, 73% of the originally recruited patients (80 out of 110 patients) completed the rehabilitation intervention. Statistically and clinically significant improvements in risk-mediating outcome variables such as aerobic capacity, total cholesterol, total cholesterol: HDL ratio, HDL, triglycerides, waist circumference, and body mass index were observed on completion of the exercise intervention. More recently, Kamm and colleagues assessed 95 patients who had survived a TIA or stroke with minor or no residual deficits both before and after a three-month hospital-based secondary prevention and outpatient neurorehabilitation program, with twice weekly therapeutic and educational sessions.[53] Vascular risk factors (SBP, DBP, body mass index, LDL, triglycerides), exercise capacity, and health-related quality of life had all significantly improved at completion of the program. These studies provide further evidence for the implementation of rehabilitation programs for TIA patients.[51,53] Prior et al concluded that cardiac rehabilitation-type exercise program is feasible, effective, and a safe secondary prevention strategy for implementation early after TIA or mild/non-disabling stroke.[51]

Early exercise engagement for stroke and TIA populations. When considering the body of evidence to date, the important question to be posed is what constitutes "early" exercise engagement? For example, Prior et al typically recruited patients 12 weeks after their TIA or mild/non-disabling stroke, but some patients were recruited as much as 285 days post their event.[51] Lennon and colleagues randomized patients to either an exercise intervention or control group, on average, five years after their stroke.[38] Stoller et al, however, define "early" as the commencement of an exercise program within six months of stroke diagnosis.[56] Clearly, there is poor consensus about what constitutes "early" and thus, what is the optimal time to start a rehabilitation program. With newly diagnosed stroke patients, the highest contributors to improved health outcomes have been suggested to be early mobilization (getting patients out of bed within 24 hours of stroke onset) and better blood pressure control.[57,58] Early mobilization has been promoted within published stroke guidelines,[59] although the practice remains controversial because of inconclusive evidence.[58,60] In the acute and sub-acute phases of stroke care, getting the balance right between diagnosis, medical interventions, and exercise rehabilitation can be challenging. Increasing our understanding of the impact of implementing rehabilitation interventions within the acute phase, whereby the effects on brain recovery, cardiovascular health, and functional restoration may be the highest, needs to be explored further. Given that stroke and TIA patients are at the highest risk of recurrent events in the first 3 months following diagnosis, there may be a "critical window'" as to when to implement a secondary prevention program. Accordingly, a recent randomized, parallel group clinical trial has examined the efficacy of early-engagement–within two-weeks of symptom diagnosis—on vascular risk factors, aerobic capacity, and recurrent events in TIA and non-disabling stroke patients.[15,52]

In the study by Faulkner sand colleagues, 60 patients diagnosed with TIA or non-disabling stroke patients were randomly allocated to either an eight-week, twice weekly exercise program, or to a usual care control group.[15,52] The exercise sessions incorporated a holistic program whereby participants took part in aerobic, resistance, balance, and flexibility training. Once a week, participants actively engaged in a group-focused education session that was designed to facilitate a greater sense of understanding and condition management among patients. These sessions focused on vascular risk factors, stroke prevention, nutrition, blood pressure, adherence to medication, stress management, and emotional and behavioral changes after TIA. The study demonstrated that on completion of the eight-week program, significantly greater reductions in SBP and total cholesterol were observed for individuals randomized to the exercise and education program.[52] Furthermore, significant improvements in aerobic capacity were also observed for those who completed the intervention. As hypertension is present in 80% of patients with acute ischemic stroke, and is independently associated with poor health outcomes,[61] coronary artery disease (CAD) and initial or recurrent strokes,[62,63] improvements in the blood pressure profile in particular, are considered very important for this population group. Based on the findings from this study, regular physical activity participation within the acute phase may be considered a useful additive treatment strategy (to prescribed medication) for newly diagnosed TIA patients.

Faulkner and colleagues also assessed the effect of the eight-week exercise program on the blood pressure (SBP, DBP), and other hemodynamic responses (heart rate, pulse pressure, double product), of newly diagnosed TIA patients during exercise.[54] This is particularly important when considering that the guidelines for the management of hypertension provide no information about the diagnosis, management, or potential clinical utility of identifying the hypertensive response to exercise.[64] In this study, 68 TIA patients completed a continuous and incremental walking test within two weeks of symptom diagnosis. Individuals were then randomized to either an eight-week exercise program or to a usual care control group before completing an identical post-intervention assessment. Participants randomized to the exercise condition experienced significantly greater reductions in the exercising heart rate, SBP (both 10–14%), pulse pressure (17–24%), and double product (26–32%) than the control group at the follow-up assessment. Although the control group typically reported a 2–3 mmHg decrease in SBP between the pre- and post-assessment sessions, the exercise group elicited a 15–17 mmHg decrease, at the corresponding walking speeds.[54]

The long-term effect of exercise participation. An important characteristic of successful behavior change is the continued engagement in lifestyle modification following

the removal of the stimulus (ie structured exercise sessions). This is where the true value and importance of an exercise program can be evaluated, as it may reduce the risk of recurrent cerebrovascular events (stroke, TIA, etc.). Although the PREVENT[65] and CRAFT[66] trials are investigating the longer-term efficacy of exercise and education programs in modifying vascular risk in TIA patients within 90 days of symptom onset, to our knowledge, Faulkner and colleagues is one of the first research groups to have reported whether the benefits observed post-intervention are maintained.[52,67] In their study, the benefits that were observed immediately following the intervention (ie SBP, aerobic capacity) were also maintained at the 3-month follow-up assessment,[45,59] and similar trends have been observed during a 12-month follow-up assessment (unpublished data). However, as sustainable, long-term behavior change is related to autonomous motivation, general expectancy, and self-efficacy, and as each of these is a significant predictor of exercise participation, such psychosocial factors should be considered in future research of this nature.[68] To date, limited research has assessed factors such as anxiety, depression, and health-related quality of life, yet this has only been considered in the short term.[38,53]

Despite the aforementioned findings, no recommendations can be drawn with respect to guiding best practice for this population group[28] because of the limited number of empirical studies and the varying nature of study designs. Larger (ie multi-site) well-designed, randomized controlled trials are needed to elucidate when exercise should be implemented and what the most efficacious form of exercise (mode, intensity, duration, etc.) is for the secondary prevention of recurrent vascular events. Each of the exercise programs alluded to in this paper featured an education and/or lifestyle strategy. For example, Lennon et al incorporated sessions on stress management,[38] whereas Prior et al provided information on risk factor and service education and delivered individual or group nutrition counseling.[51] Faulkner and colleagues implemented once a weekly education session that covered a breadth of lifestyle information, including risk factors for stroke, dietary, and smoking advice, and cognitive/behavioral effects post-stroke/TIA.[52] As these interventions were a composite of both exercise and education, it is difficult to establish whether the positive changes observed in the aforementioned outcome measures, both short[38,51–53] and long terms,[52] were because of an increase in regular, structured physical activity; or because of an elevated awareness in the need to improve lifestyle factors, as was highlighted in the education sessions (ie diet). Furthermore, as cardiac rehabilitation-type exercise programs incorporate participation in both aerobic and resistance exercises, research is yet to establish whether the favorable changes in CVD risk factors and aerobic fitness are more so because of one type of exercise rather than another. Accordingly, future research should therefore consider the individual effect that exercise (ie aerobic versus resistance versus aerobic and resistance) and education has on vascular risk factors and fitness in such population groups. It is also of interest to note that research studies that have investigated the aerobic fitness of TIA or mild/non-disabling stroke patients have typically incorporated submaximal exercise tests[38,52] and/or have not used online gas analysis.[51,52] As predictive equations have inherent error, future research should more accurately measure oxygen consumption and aerobic capacity of these population groups before and after a given intervention. Furthermore, the RCTs and prospective studies discussed in this paper did not explore the physiological mechanisms as to why exercise may have an important effect on cardio- and cerebrovascular health within this population group (ie arterial stiffness, cerebral blood flow regulation). This may be pertinent when tailoring specific exercise programs for patients post-stroke or TIA.

Conclusion

In conclusion, recent research has demonstrated that exercise participation in the acute or sub-acute phase may provide statistically and clinically significant changes in vascular risk factors (blood pressure, total cholesterol, etc.) and aerobic fitness, in patients diagnosed with TIA or mild/non-disabling stroke. Although research in this area of interest is in its infancy, structured exercise participation, similar to that incorporated during a cardiac rehabilitation program, has shown to be a feasible, effective, and safe secondary prevention strategy for this population group. Nevertheless, future research should consider the use of larger multi-site randomized controlled trials, differing exercise interventions (ie mode, intensity, duration), and psychosocial effects of structured exercise participation. Furthermore, the short- and long-term implications of these aforementioned factors need to be considered.

Author Contributions

Conceived and designed the experiments: JF. Analyzed the data: JF, DL, LS. Wrote the first draft of the manuscript: JF. Contributed to the writing of the manuscript: JF, DL, LS. Agree with manuscript results and conclusions: JF, DL, LS. Jointly developed the structure and arguments for the paper: JF, DL. Made critical revisions and approved final version: JF, DL, LS. All authors reviewed and approved of the final manuscript.

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As a requirement of publication the authors have provided signed confirmation of their compliance with ethical and legal obligations including but not limited to compliance with ICMJE authorship and competing interests guidelines, that the article is neither under consideration for publication nor published elsewhere, of their compliance with legal and ethical guidelines concerning human and animal research participants (if applicable), and that permission has been obtained for reproduction of any copyrighted material. This article was subject to blind, independent, expert peer review. The reviewers reported no competing interests. Provenance: the authors were invited to submit this paper.

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