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ISCHEMIC HEART DISEASE (D MUKHERJEE, SECTION EDITOR)

Lifestyle Interventions to Prevent Cardiovascular Events After Stroke and Transient Ischemic Attack

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Abstract

Purpose of Review To summarize lifestyle interventions including pharmacological and non-pharmacological methods targeting modifiable risk factors and their impact on the future cardiovascular events in patients who have suffered transient ischemic attack (TIA) and/or ischemic stroke (IS).

Recent Findings The latest research indicates that secondary prevention measures can decrease the risk of recurrent stroke, cardiovascular events, and even death. Modifiable risk factors also require behavioral change which can be challenging.

Summary There is limited data demonstrating the impact of lifestyle interventions, alone or as part of an integrated care pathway, based on cardiovascular events. There is some support for lifestyle interventions such as increased exercise participation that when delivered as part of a comprehensive care package post stroke leads to minor reductions in blood pressure. High-quality, robust trials are required with longer-term follow-up and clear documentation of mortality, morbidity, and cardiovascular risk profile outcomes.

Keywords Lifestyle · Transient ischemic attack · Stroke

Introduction

There is an increased risk of cardiovascular events following a transient ischemic attack (TIA) or stroke [1•, 2•]. High blood pressure, diabetes, high cholesterol, obesity, and smoking are the leading causes of stroke and coronary heart disease (CHD). One in three adults in the USA has at least one of these diseases or habits [3].

A recent meta-analysis of 58 studies found that the risk of myocardial infarction (MI) following TIA/ischemic stroke (IS) was 1% and 3.6% per year in patients with or without history of CHD respectively. Patients with a prior history of TIA or IS, presence of hypertension, CHD, and peripheral artery disease (PAD), and male gender were twice as likely to have a MI [4]. In another systematic review, the annual risk of MI after TIA or IS was found to be 2.2%, with high mortality following the initial event and a rise in mortality about 3 years thereafter due to suspected decline in pharmacology compliance and reduced attention to lifestyle factors [2•].

Risk factors for recurrent cardiovascular events can be classified into three major groups: *Non-modifiable* risk factors such as age, gender, ethnicity, and family history; *Medically modifiable* risk factors like hypertension, hyperlipidemia, and

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diabetes; and *Behaviorally modifiable* risk factors like tobacco, physical activity, and diet which can be modulated by changes in lifestyle [5].

There is a clear evidence that secondary preventative measures can help reduce recurrent stroke risk, CHD, and even death [6]. However, it is still not clear which of the lifestyle factors is most effective in reducing the risk of cardiovascular events after stroke and TIA. Our objective was to perform a literature search and summarize pharmacological and lifestyle interventions and their impact on future cardiovascular events in patients who have previously suffered TIA and/or IS.

Modifiable Risk Factors Interventions and Their Impact on Cardiovascular Events

Hypertension

It is the single most important vascular risk factor. Blood pressure is the most consistent and powerful predictor of cardiovascular disease, in both primary and secondary prevention. The incidence of IS and cardiovascular events has been reported to decrease with secondary prevention of hypertension [4]. The Perindopril Protection Against Recurrent Stroke Study (PROGRESS) randomized 6105 patients with a history of TIA or stroke (ischemic or hemorrhagic) to active treatment with a perindopril-based regimen in addition to other antihypertensive medications or placebo. Over 4 years, the relative risk (RR) of stroke was reduced by 28% with a similar RR reduction of 26% for all-cause cardiovascular morbidity [7].

In a meta-analysis, Deijle et al. found that interventions involving a cardiovascular fitness program resulted in a significant reduction in SBP [8••]. It was postulated that exercise training decreases systemic vascular resistance and thereby reduces blood pressure. Their meta-analyses showed that trials with an intervention that lasted longer than 4 months and interventions that used > 3 behavior change techniques were more effective in reducing SBP. Behavior change techniques utilized coordinated sets of activities in the form of education, counseling programs, self-control, motivation etc., which target specified behavior patterns of the individual [9, 10].

In a similar way, a systematic review and meta-analysis performed by Wang et al. demonstrated that exercise interventions resulted in significant reductions in both SBP (− 4.30 mmHg) and DBP (− 2.58 mmHg), particularly when initiated within 6 months of stroke or TIA and when combined along with health education [11]. Based on the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure, adults not previously treated for hypertension who experience a stroke or TIA and have an established BP of 140/90 mmHg or higher should be prescribed antihypertensive treatment a few days after the index event to reduce the risk of recurrent stroke and other vascular events and a BP goal of less than 130/80 mmHg may be reasonable [12].

Dyslipidemia

The American Heart Association/American College of Cardiology Guidelines recommend statin therapy with intensive lipid-lowering effects to reduce the risk of stroke and cardiovascular events [13]. Though statins are still the first-line therapy, 2017 update of ACC consensus provided the guidance for the use of non-statins in certain subsets of patients as an adjunct to reduce the risk of atherosclerotic cardiovascular disease (ASCVD) [14]. Currently, there are no studies which can determine the long-term efficacy of non-statin monotherapy or combination therapies in reducing the risk of ASCVD especially in patients with statin intolerance.

A randomized control trial by Kono et al. in 70 patients with acute non-cardioembolic mild ischemic strokes demonstrated that lifestyle interventions like exercise training, salt restriction, and nutrition advice for 24 weeks resulted in a significant reduction in SBP, a decrease of 13.0 mmHg, and an increase of 11.6 mg/dl in high-density lipoprotein cholesterol (HDL-C) levels. After a follow-up of 2.9 years, 1 patient (2.8%) in the intervention group developed angina pectoris compared with 12 in the control group (34.3%; 5 with stroke recurrence, 6 with MI, and 1 with angina pectoris) [15].

Diabetes Mellitus

Disorders of glucose metabolism have a high prevalence in patients with cerebrovascular disease. Diabetes mellitus has been associated with more than 8% risk of the first IS [16]. Twenty-eight percent of patients with IS have pre-diabetes while up to 45% of patients have overt diabetes. So far, no major trials have examined the impact of interventions for pre-DM or DM in the secondary prevention of cardiovascular events after stroke specifically. A meta-analysis of 58 studies conducted by Boulanger et al. on patients who had TIA or IS demonstrated no difference in the risk of MI in patients with a history of diabetes mellitus (RR = 1.14, 95% CI = 0.71–1.76) compared with those without it [4].

Management of patients with DM or pre-DM and stroke is based on studies done in non-stroke or mixed populations. Lifestyle interventions and pharmacotherapy can however prevent progression of impaired glucose tolerance (IGT) to DM [17].

Obesity

According to the Centers for Disease Control and Prevention, one is considered obese if the individual's body mass index is greater than 30. The prevalence of obesity among US adults

was 39.8% in 2015–2016 [18]. Obesity has been associated with an increased prevalence of vascular risk factors. Obesity is diagnosed in 18 to 44% of patients with a recent TIA or IS, although precise estimates are available from only a few studies, and estimates are likely to vary from country to country and region to region within the same country [10].

Achieving and maintaining optimal weight is difficult. Preventative diet advice from the family physician is often inadequate. Intensive behavior-based counseling is required. Weight loss can also be achieved with drugs or bariatric surgery. Unfortunately, there are very few randomized studies reporting the effect of any of these interventions on cardiovascular events post stroke or TIA. The Look AHEAD (Action for Health in Diabetes) study is the only randomized controlled trial which was adequately designed to examine the effect of behavioral interventions for weight loss on the risk of cardiovascular events. However, the modest weight loss achieved in the study (i.e., 6% of initial body weight) did not seem to reduce the risk for cardiovascular outcomes after a mean follow-up of 9.6 years [19].

Sleep Apnea

Sleep apnea is a common disorder affecting 20% of the general population and around 50–70% of stroke patients [20]. Obstructive sleep apnea (OSA) may predate the stroke, become worse during the acute phase of the stroke, and continue to persist after the acute phase. Anecdotally, continuous positive airway pressure (CPAP) has helped to improve recovery from stroke and also decreased the risk of recurrent stroke. Preliminary randomized trials of CPAP therapy after IS have shown an improvement in stroke impairment scales, depressive symptoms, motor recovery, sleepiness, and the time until the appearance of cardiovascular events [20].

A prospective study involving 95 patients demonstrated that CPAP treatment during 18 months in patients with an apnea-hypopnea index (AHI) > or = 20 afforded significant protection against new vascular events after ischemic stroke [21]. Parra et al. conducted an RCT on patients with a first-ever IS and moderate-severe OSA with an AHI ≥ 20. Patients were assigned randomly to the nasal CPAP ($n = 71$) vs a control group ($n = 69$). After a 5-year follow-up, patients in the nasal CPAP group had significantly higher cardiovascular survival (100 versus 89.9%; $P = 0.015$) [22].

General Lifestyle Interventions

Diet

There is a lower risk of developing heart disease, stroke, and hypertension in dietary patterns characterized by a high intake of fruits and vegetables [23]. In a RCT performed by Kono et al., dietary modification, including low-saturated fat, calorie restriction, and potassium-rich foods in addition to other lifestyle modifications like exercise and salt reduction, showed a significantly reduced stroke recurrence and other cardiovascular events like MI, PAD, and angina pectoris during a 2.9-year follow-up [15].

Based on the data published in various studies including randomized and non-randomized, observational studies—Mediterranean diet has proven to be beneficial for both primary and secondary prevention of cardiovascular disease [24].

In the PREDIMED trial (Prevención con Dieta Mediterránea), the primary outcome of cardiovascular death, myocardial infarction, or stroke showed an event rate of 8.1 events/1000 person-years in the Mediterranean diet plus olive oil group which was similar to 8.0 events/1000 person-years in the Mediterranean diet plus nuts group. These results were statistically significant when compared with 11.2 events/1000 person-years in the control diet. Similar trends were also seen in the stroke rates among the three groups [25].

The beneficial effects may be attributed to the synergistic interplay between various nutrients found in the Mediterranean diet that modulates intermediate pathways of cardiometabolic risks, such as cholesterol, insulin sensitivity, oxidative stress, free radicals, and inflammatory cascade [26].

Exercise

Cardiorespiratory training after a stroke reduces disability, and this may be mediated by improved balance and mobility [27]. A recent meta-analysis that included 13 studies reported physical activity as an outcome measure in post-stroke patients [8••]. Some of these studies used either behavior change interventions [28] or cardiovascular fitness intervention or a combination of both interventions. About half of these studies showed an improvement in the physical activity level, and almost 1/3 of the studies showed improvement in cardiorespiratory fitness as measured by maximal oxygen uptake or using the 6-minute walk test. Despite improved physical activity tolerance, there is no direct evidence to show the effect of exercise on cardiovascular event post stroke.

A meta-analysis of 48 RCTs including a total of 8940 patients by Taylor et al. has reported a significant 3.2-mmHg decrease in SBP in patients with CHD, but interestingly no significant difference in DBP after an exercise-based cardiac rehabilitation program was observed. This study demonstrated that cardiac rehabilitation was associated with a significant reduction in all-cause mortality and total cardiac mortality [29].

Stress

Work stress related to profession and long working hours are associated with a moderately elevated risk of incident of CHD

and stroke according to a meta-analysis which included 600,000 men and women from 27 prospective cohort studies in Europe, the USA, and Japan [29]. The excess risk for exposed individuals is 10–40% compared with those free of common work stressors like job strain, long working hours, and job insecurity. However, due to the limited interventional evidence on benefits, harms, and cost-effectiveness, the US Preventive Services Task Force has not made any definitive recommendations for the primary prevention of cardiovascular disease via workplace stress reduction.

Cigarette Smoking

Cigarette smoking is another independent risk factor for the first IS. The Cardiovascular Health Study has discussed the substantial increased risk of stroke recurrence among elderly smokers [30]. Research has shown that exposure to tobacco smoke or passive ("secondhand") smoke increases the risk of stroke [31]. However, no clinical trials have yet studied the effectiveness of smoking cessation in the secondary prevention of cardiac events after stroke or TIA. Such trials are unlikely to be initiated considering our current knowledge about the harmful effects of smoking. However, a recent meta-analysis looking into temporal trends in ischemic stroke/transient ischemic attack patients has shown that there was no significant difference in the risk of MI in patients with a history of current smoking (RR = 1.21, 95% CI = 0.83–1.73) compared with those without a history of smoking [4].

Challenges in Making Therapeutic Lifestyle Changes

Major public organizations and government agencies like the American Heart Association (AHA), Centers for Disease Control and Prevention, and the National Institutes of Health (NIH) have periodically come up with statistical updates to target the general population, healthcare workers, and political and policymakers with up-to-date statistics and strategies to promote cardiovascular health. The ideas like AHA's Life's Simple 7 emphasizes on core health behaviors (smoking, physical activity, diet, and weight) and health factors (cholesterol, blood pressure, and glucose control) for healthy living in all age groups [32].

Despite the initiatives, notable challenges that patients still frequently face are lack of knowledge about exercise and diet and lack of time and motivation [33]. The level of motivation is directly affected by the immediate consequences of their disease to some extent [34]. Families also play a major role by motivating the patients to adhere to their goals [33]. Post-stroke disability compromises one's ability to maintain both cardiorespiratory and physical fitness [35]. Patients may need more assistance from their family physicians or primary care physicians about lifestyle changes especially in setting realistic goals and suitable recommendations [36].

Physicians treating such patients may also face challenges in terms of time constraints to educate patients, inadequate physician knowledge about diet, and exercise counseling.

The physicians in some studies have acknowledged this fact and stated a need for education and awareness to overcome their deficiencies [37, 38]. Introducing the concept of action planning—where an agreement is made between a clinician and patient that the patient will make a specific behavior change has shown significant benefits to the patients [39]. In addition, various review articles, guidelines, and online resources from professional organizations may help physicians with patient health education counseling skills [40, 41].

Technology such as the Internet and the use of smartphones has revolutionized the idea of health promotion research and practice. A number of randomized controlled trials showing the effectiveness of smartphone apps in improving diet and nutrition and controlling weight could not reach significance. On the bright side, mobile apps can be effective in promoting healthy eating and weight loss which is a low-cost intervention for improving diet and nutrition and addressing obesity in the general population [42].

Conclusions

Published studies and their meta-analysis indicate that, currently, there is a lack of data or limited data demonstrating the robust impact of lifestyle interventions, alone or as part of an integrated care pathway, based on cardiovascular events. There is some support for lifestyle interventions for increased exercise participation and when delivered as part of a comprehensive care package post stroke for minor reductions in blood pressure. High-quality, robust trials are required with longer-term follow-up and clear documentation of mortality, morbidity, and cardiovascular risk profile outcomes. There are no studies targeting patients in the acute phase and those with severe disability post stroke. Research with randomized controlled trials in these areas is required in the future.

Compliance with Ethical Standards

Conflict of Interest Anantha R. Vellipuram, Gustavo Rodriguez, Prashanth Rawla, Alberto Maud, Salvador Cruz-Flores, and Rakesh Khatri declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- •• Of major importance

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