Stroke Prevention

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Abstract

Stroke has three main subtypes - ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage. The most common stroke subtype is ischemic stroke, making up about 88% of strokes. Many of these strokes may be prevented by lifestyle modifications. These lifestyle modifications include engaging in physical activity, dietary changes such as the Mediterranean diet, smoking cessation, and avoiding substance abuse. Addressing medical conditions such as diabetes, hypertension, lipid management, sleep apnea, and atrial fibrillation will also have a major impact on stroke prevention. In addition to stroke prevention, these strategies help with overall brain health, which may also have an impact on neurological degenerative diseases such as Alzheimer's disease.

Introduction

Each year it is estimated that approximately 800,000 individuals in the United States suffer a stroke. Stroke has three main subtypes - ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage. The most common stroke subtype is ischemic, making up about 88% of strokes. Ischemic stroke occurs by acute interruption of blood flow resulting in brain tissue injury. This is best visualized acutely on MRI diffusion weighted image sequences. A transient ischemic attack (TIA) is the same process without resulting tissue injury; therefore, no abnormality is seen on an MRI diffusion weighted image. Intracerebral hemorrhage, at approximately 10%, is the next most common stroke followed by subarachnoid hemorrhage at about 2%. Prevention strategies discussed in this article are going to be confined to the ischemic stroke subtype; however, risk factor modification strategies are oftentimes applicable to the other two stroke subtypes.[1,2]

There has been a trend towards reduction of stroke incidence from 8.7% in the 1960s to 5.0% in the 2000s. This is thought to be secondary to improved blood pressure control and the use of antiplatelet medications.[1] The optimal stroke prevention strategy for an individual depends on the underlying etiology of their stroke. In general, management of vascular risk factors, including management of diabetes, smoking cessation, lipid management, hypertension management, as well as lifestyle modification provide the foundation for prevention of stroke. Lifestyle factors such as low-sodium, Mediterranean diet and physical activity may provide the greatest benefit for primary and secondary prevention. Addressing these factors also helps maintain optimal brain health.

Primary Prevention

Primary prevention of stroke involves identification of specific factors associated with vascular disease. These include the presence or absence of diabetes, hypertension, current smoking, cholesterol, race, and sex. Cardiovascular risk assessment scores have been shown to be very useful for targeting individuals that are at risk for a stroke. One such tool is the American Heart Association/American College of Cardiology Vascular Risk calculator (ASCVD Risk Estimator

Plus). This calculator uses age, sex, race, systolic and diastolic blood pressure, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), history of diabetes, smoking history, hypertension treatment, statin usage, and aspirin treatment to give a 10-year atherosclerotic cardiovascular disease risk score.[3] This tool is oftentimes used to start a conversation with a patient to help with motivation in controlling these risk factors.

Physical Activity

Physical inactivity has been a well-defined and modifiable risk factor for cardiac disease and stroke. In the Northern Manhattan Stroke Study, a dose response relationship showing more intensive physical activity had greater stroke reduction compared to light and moderate physical activity. It is felt that exercise itself plays a part through potential factors such as anti-inflammatory effects, but also the modification of other associated risk factors such as reduction in blood pressure, body mass index (BMI), lipid levels and better diabetic control.[4]

Diet

Diet and nutritional studies have identified the protective effects from stroke by regular consumption of fish,[5] high consumption of fruit and vegetables,[6] following a Mediterranean diet,[7] and the Dietary Approaches to Stop Hypertension (DASH) diet.[8] The Mediterranean diet is high in the monounsaturated/saturated fat ratio, using olive oil as a main cooking ingredient. Consumption of other traditional foods high in monounsaturated fats such as tree nuts and other plant-based foods including fruits, vegetables, legumes whole grains, and cereals; increased consumption of fish; low consumption of meat and meat products; and discouraging the consumption of red and processed meats have been shown to be beneficial. Low alcohol consumption should be encouraged. The vascular-healthy diet moderates the consumption of milk and dairy products, and discourages soda drinks, pastries, sweets, commercial bakery products and spread fats. It also emphasizes consumption of less than 1500 mg of sodium per day. The reader is encouraged to go the American Heart Association website (https://www.heart.org) for further recommendations.

Tobacco

Tobacco use is the number one preventable cause of death in the United States and globally. Cigarette smoking is the most common form of tobacco use and is a major risk factor for stroke. Other forms of tobacco use are becoming increasingly popular. Electronic cigarette use has risen dramatically among young adults. Its use among young people has increased by 900% from 2011 to 2015. Compared to non-users e-cigarette users had higher adjusted odds of stroke.[9] The risk of ischemic stroke has been estimated to be twofold higher in those individuals who smoke, and there is a threefold higher risk of subarachnoid hemorrhage. The risk of stroke is reduced when those individuals quit smoking. Between two to five years after cessation of smoking, the stroke risk approaches those who have never smoked.[10]

Substance Abuse

Alcohol consumption and ischemic stroke have a J-shaped relationship, regardless of sex. Stroke risk is increased with heavy alcohol consumption (greater than three drinks per day for men and greater than two drinks per day for women).[11] It is recommended that patients with an ischemic stroke or TIA who drink more than two alcoholic drinks a day (men) or more than one alcoholic

drink (women) be counseled to eliminate or reduce their consumption of alcohol to reduce stroke risk.[1] Acute ischemic stroke hospitalization is higher among cannabis users, and the US Centers for Disease Control and Prevention identified that young adults with recent cannabis use have higher odds of stroke compared with nonusers.[12] In patients with stroke or TIA who have a substance use disorder (drugs or alcohol), specialized services are recommended to help manage this dependency.

Diabetes

Diabetes is defined as a heterogeneous mix of health conditions characterized by blood glucose dysregulation. The most common forms are type 2 diabetes, which affects 90 to 95% of those with diabetes, and type 1 diabetes which constitutes 5 to 10%. Diabetes is defined as having a fasting glucose of greater than 126, a 2-hour post challenge glucose greater than 200, or a hemoglobin A1c greater than 6.5. Prediabetes is defined as a fasting glucose 100-125, 2-hour glucose test of 140-199, hemoglobin A1c of 5.7-6.4.

Type 1 diabetes is an autoimmune disorder that results in absolute insulin deficiency. Type 2 diabetes results from progressive impairment of insulin sensitivity and pancreatic insulin secretion. The pathophysiology of prediabetes is the same, with the only difference in the blood sugar level.

In Delaware, more than 98,000 individuals (about the seating capacity of the Los Angeles Memorial Coliseum), reported that they had been diagnosed with diabetes. In 2017, approximately 95,000 Delawareans reported that they had been diagnosed with prediabetes. Delaware's prevalence of diagnosed diabetes, 13%, is greater than the national average of 11%.[13] Diabetes prevalence is increasing in Delaware: from 2002 to 2019 Delaware's adult diabetes prevalence rate rose from 8% to 13%, and at the projected rate it is estimated to be over 121,000 residents in the State of Delaware by 2030.[14]

Diabetes increases the risk of stroke nearly three-fold and disproportionately affects the elderly and minority population.[15] The duration of diabetes increases the risk of stroke by 3% per year.[16] Prediabetes is present in approximately 30% of patients with acute ischemic stroke.[17] Progression of prediabetes to diabetes can often be prevented by diet, weight control and exercise.

Despite the fact that diabetes is a disease having its pathophysiological effects related to impaired blood glucose control, there has been extremely limited data to support tight glucose control and the reduction of stroke risk for other cardiovascular events. In the Action to Control Cardiovascular Risk and type 2 Diabetes (ACCORD) study, patients with a mean hemoglobin A1c of 8.1% assigned to intensive glucose control with a target hemoglobin A1c of less than 6 were compared to a standard control group with hemoglobin A1c of 7.0-7.9. The study was stopped secondary to higher mortality rates in the intensive treated group. There was no difference in the risk of nonfatal stroke.[18] Further studies are needed.

In patients who have had an ischemic stroke or TIA and have diabetes, the goal for glycemic control should be individualized. This should be based on the risk for adverse events, patient characteristics, and patient preferences. For most patients, achieving a hemoglobin A1c of 7% is recommended to reduce the risk of microvascular complications. The American Diabetes Association (ADA) have revised their algorithms for the management of type 2 diabetes. An evidence-based consensus report by the ADA and the European Association for the Study of

Diabetes recommends metformin and comprehensive lifestyle changes as the first-line therapy.[19] Because of new classes of glucose lowering medications that also prevent clinical vascular disease, the ADA recommends that in patients with ischemic strokes, glucagon-like peptide 1 (GLP-1) receptor agonists should be added to metformin, independent of baseline hemoglobin A1c. When concern for heart failure or chronic kidney disease predominates, the addition of a sodium glucose cotransporter 2 inhibitor to metformin is recommended. Through shared decision making, the treating provider should help the patient decide if the GLP–1 receptor agonist or the sodium glucose co-transporter 2 inhibitor is right for them. Costs, side effects, desired weight loss, aversion to injection therapy, and desire to reduce risk for hypoglycemia are factors that should be weighed in this discussion.

Hypertension

Hypertension is one of the most modifiable risk factors for ischemic and hemorrhagic stroke. Data from randomized clinical trials and large meta-analysis provide compelling evidence that neurologically stable patients with cerebrovascular disease benefit from a blood pressure goal of less than 130/80 mmHg, and that blood pressure targets for stroke prevention should be more aligned with targets for prevention of other cardiovascular conditions. Treatment of hypertension includes weight reduction, aerobic activity, dietary modification including daily sodium consumption of less than 1500 mg, and medications. Diuretics, angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blocking medications have demonstrated benefit in multiple trials in stroke prevention. Calcium channel blockers are recommended to treat hypertension, but there is limited data on their efficacy for secondary stroke prevention. However, if the use of calcium channel blockers is reasonable for patients who are having uncontrolled hypertension, this may be an option.[13,20] The Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment (RESPECT) trial, Prevention After Stroke- Blood pressure (PAST-BP) trial and the Prevention of Decline in Cognition After Stroke (PODCAST) trial compared intensive control of systolic blood pressure ranges from less than 120-130 mmHg with standard blood pressure control targets of less than 140-150 mmHg in patients with prior strokes. These trials all reported significant tendencies toward lower recurrent stroke rates in the intensive treatment groups.[21–23] The exception to this may be in those patients with significant small vessel disease and/or significant intracranial atherosclerotic disease.

The degree of blood pressure lowering appears to be more important for the risk reduction of stroke than the class of antihypertensive agent used.[24] The recommended threshold of blood pressure greater than 130/80 mmHg for starting hypertensive medication is due to the baseline blood pressure in patients of cerebrovascular disease studied in the above mentioned trials. There are, however, some unanswered questions concerning blood pressure management. Optimal blood pressure target for the very elderly population and for those individuals with extensive small vessel disease is unknown. The optimal blood pressure target for patients with diabetes and stroke and the optimal timing to begin blood pressure lowering after stroke need further study.

Lipid Management

Most studies have found high total cholesterol to be a risk factor for ischemic stroke. In the multiple risk factor intervention trials comprised of greater than 350,000 participants, relative

risk of death resulting from non-hemorrhagic stroke increased progressively with each higher level of serum cholesterol.[25] In the women's Pulling project, which included 24,000 US women less than 55 years of age with no previous cardiovascular disease, and the Women's Health study, a prospective study of 27,000 US women greater than 45 years of age, higher cholesterol levels were associated with increased risk of ischemic stroke.[26,27] However, in the Atherosclerotic Risk In the Community (ARIC) study of 14,000 middle-aged men and women free of cardiovascular disease, the relationship between lipid values and incident ischemic stroke was weak.[28] The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial and the Treat Stroke to Target trial evaluated lipid lowering therapy in patients after ischemic stroke and found significant benefit from cholesterol-lowering therapy in preventing vascular events including stroke.[29] SPARCL found atorvastatin 80 mg daily reduced stroke recurrence in patients without another indication for statin therapy. The Treat Stroke to Target trial confirmed that target LDL less than 70 was superior to target of 90-110 for preventing major cardiovascular events. These specific treatment trials and numerous other randomized clinical trials of lipid lowering drugs indicate that high risk patients with atherosclerotic cardiovascular disease should receive high intensity statin therapy. If the LDL-C remains greater than 70 on maximally tolerated statin therapy, it may be reasonable to add ezetimibe and then a PCSK9 inhibitor if the patient is deemed to be at very high risk.[29] Accordingly, the 2018 American Heart Association/American College of cardiology guidelines on management of blood cholesterol for high intensity statin therapy recommend atorvastatin 80 mg daily or rosuvastatin 20 mg daily.[1]

Sleep Apnea

Sleep apnea is associated with an increased risk of cardiovascular disease and stroke. In a longitudinal study it was found that patients with severe obstructive sleep apnea doubled their risk of stroke.[30] The ASA guidelines recommend patients with ischemic stroke or TIA and obstructive sleep apnea be treated with continuous positive airway pressure (CPAP). This can be beneficial for improved sleep apnea, blood pressure, sleepiness, and other apnea related outcomes. In addition, treatment of sleep apnea is felt to be important in maintaining overall good brain health.

Atrial Fibrillation

Nonvalvular atrial fibrillation (AF) is an important and treatable risk factor for stroke. In patients with nonvalvular AF and stroke or TIA, oral anticoagulation with apixaban, dabigatran, edoxaban, rivaroxaban or warfarin is recommended to reduce the risk of stroke, regardless of whether the AF is permanent, paroxysmal, or persistent. In patients with AF and stroke or TIA who do not have moderate to severe mitral stenosis or a mechanical heart valve, apixaban, dabigatran, edoxaban, or rivaroxaban, are recommended over warfarin to reduce the risk of stroke. These recommendations are made based on the evidence from four large, randomized trials comparing the direct oral anticoagulants versus the vitamin K antagonist, warfarin.[31–34]

There are other prevention strategies for specific stroke types that go beyond the scope of this article. The reader is advised to read the American Stroke Association guidelines, which are continually updated, for specific recommendations.

Conclusion

Risk factor modification is vital for both primary and secondary stroke prevention. In order to achieve this auspicious goal, clinicians and patients must work together to create a comprehensive prevention and treatment plan. Communicating the importance of lifestyle modification and medical compliance is vital. The rewards of successfully making these changes are great, not only in stroke prevention, but in improving overall brain health, and preventing cognitive decline and allowing patients to remain independent and productive.

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