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How to reduce the risk of ischemic stroke? Overview of recommendations and their effectiveness

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ABSTRACT

Stroke is a very serious life-threatening condition. It is the second cause of death worldwide [5], while even in non-fatal cases it can result in severe disability and complications [5, 8].

Of all cases, ischaemic stroke is the most common, accounting for 87% of all ischaemic stroke cases [4].

Some hope is offered by the fact that modifiable risk factors are responsible for 90% of ischaemic stroke cases [7, 14]. Consequently, a number of recommendations have been made regarding health-promoting behaviours and treatment goals for diseases associated with an increased risk of stroke in high-risk populations.

The aim of this work is to present risk groups, i.e. patient groups at higher than population risk of stroke, and to assess the effectiveness of the recommendations and the impact of their application on stroke risk.

Methods and materials

We reviewed the literature available on PubMed and Google Scholar using the words: Stroke, ischemic stroke, prevention, epidemiology

Summary

The data analysed clearly indicate that modifiable risk factors are responsible for the majority of cases (up to 90%) of stroke. Identifying risk groups on the basis of the Life's Essential 8 proposed by the American Heart Association for the prevention of cardiovascular disease, yields measurable results in lowering the risk of stroke among patients. Clearly defined standards can also set therapeutic targets for the treatment of conditions and diseases strongly associated with stroke risk and further improve population health.

Primary care plays a very important role, as it is often the patient's first contact with the health care system.

Keywords: Stroke, ischemic stroke, prevention, epidemiology

Introduction

According to the 1970 definition by the World Health Organization, a stroke is a sudden onset of rapidly developing clinical symptoms of focal or generalized brain dysfunction, with symptoms lasting at least 24 hours (or leading to death), having an exclusively vascular origin. According to this definition, a stroke includes cerebral infarction (ischemic stroke), intracerebral haemorrhage, and subarachnoid haemorrhage [2].

The definition has been updated by American Heart Association/American Stroke Association in 2013 when the silent infarctions (inclusive of cerebral, spinal and retinal) and silent haemorrhages have been added to the definition [3].

Stroke is an immediate life-threatening condition. It is the second most common cause of death worldwide [5] and even in non-fatal cases can result in serious complications. A study of 220 patients over the age 65 with ischemic stroke, indicated that they suffered from the following complications: hemiparesis (50%), cognitive deficits (46%), hemianopia (20%), aphasia (19%), sensory deficits (15%) [8].

Stroke is the third leading cause of death and disability combined [6].

Unfortunately from 1990 to 2019, the absolute number of incident strokes has increased by 70%, from 12.2 million to 101 million. In addition, it should be remembered that approximately 87% of all strokes are ischemic strokes[4]. Number of deaths from stroke has increased by 85% and it resulted also in increase of DALYs due to stroke by 32% [6].

These figures are worrying, but there is some hope of reversing the trend in the fact that 10 modifiable risk factors are responsible for 90% of stroke risk [7,14] The factor that correlates most closely with the increase in stroke incidence in recent years is obesity [6].

Therefore, primary prevention and education of the public about healthy lifestyles and the health consequences of stroke is very important. The aim of this study is to identify factors and behaviours that can be applied in primary prevention of ischaemic stroke and to evaluate their effectiveness.

Modifiable Risk Factors and prevention

Correctly identifying and minimising risk factors is the most important step in the prevention of cardiovascular disease (CVD) [10]. Modifiable cardiovascular risk factors have been grouped by the American Heart Association into eight main categories. The clear identification of risk factors is intended to promote an approach based on the prevention rather than the treatment of certain disease entities. In-depth analysis resulted in defining 8 categories, such as: diet, physical activity, nicotine exposure, sleep health, body weight, blood lipids, blood glucose and blood pressure. The analysis of the factors resulted in the definition of Life's Essential 8, which is a good model of therapeutic goals and behaviours that may influence the occurrence of stroke [9].

1 Life's Essential 8. Source *https://pubmed.ncbi.nlm.nih.gov/35766027/#&gid=article-figures&pid=figure-1-uid-0*

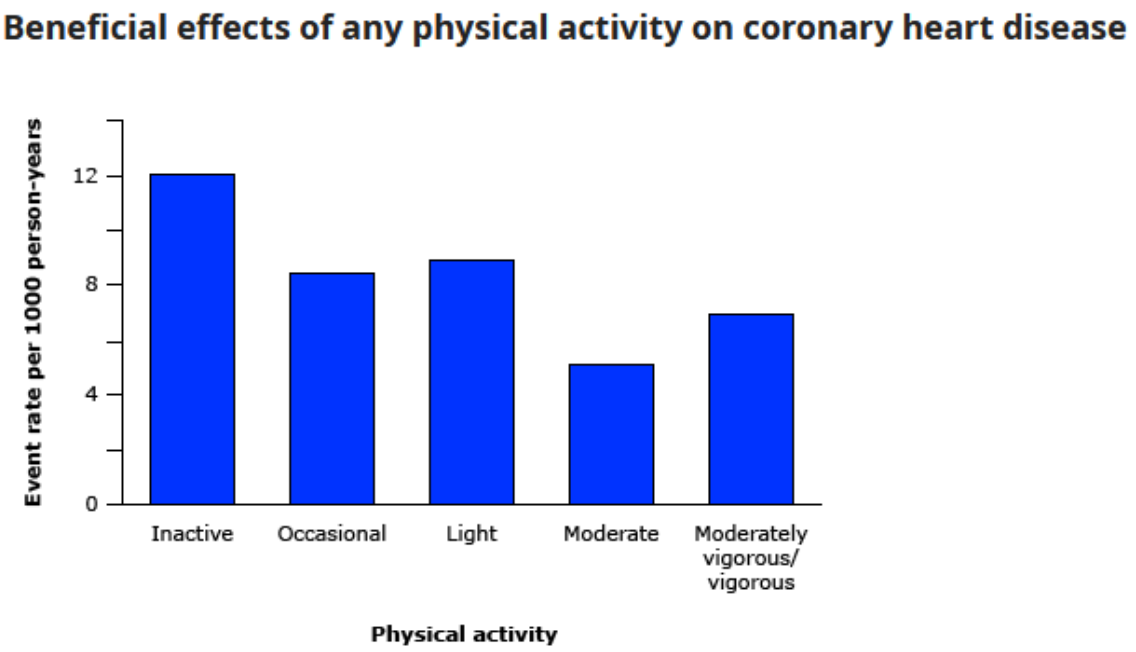
Diet

Diet has a very important place among risk factors because it can indirectly influence other parameters such as blood glucose levels, body mass index, lipid concentrations or blood pressure [12]. Over recent years, the importance of this factor has increased as the trend in weight and Body Mass Index has increased in the general population [6,]. Adjusting patients diet is very complex task. It requires reinforcing positive eating patterns, such as high intake of vegetables, fruits, legumes, nuts and also non-fried fish [11] but also drawing attention to areas for improvement which is reducing intake of animal protein, oils with polyunsaturated fats and other foods, excessive consumption of which may be associated with an increased cardiovascular risk, for example: processed food, red meat, sugar, food with high sodium levels. The type of diet with the greatest impact on cardiovascular risk reduction among patients is the Mediterranean diet with folic acid and B-complex vitamins [1,13].

Physical activity

The protective effect of physical activity on stroke risk is indicated in the scientific literature. People who regularly participate in sport have a significantly lower risk of stroke and a lower stroke-related mortality compared to those with a sedentary lifestyle.

It is highly recommended to have 150 minutes of moderate intensity exercise or 75 minutes of vigorous-intensity exercise per week. Muscle strengthening activities are recommended twice a week [15]. However data clearly indicates that any type of physical activity is better for lowering cardio-vascular risk than being inactive. Graph below clearly indicates that any type of physical activity significantly reduces events of coronary heart disease and cardio-vascular risk. Coronary heart disease and stroke are categorised as cardiovascular diseases that are included together in the SCORE 2 risk scale due to their common ethology, therefore factors that reduce the risk of coronary heart disease will reduce the risk of stroke.



2 Beneficial effects of any physical activity on coronary heart disease. Data from: Wannamethee SG, Shaper AG, Alberti KG. Arch Intern Med 2000; 160:2108.

Blood glucose

Increased blood glucose levels most commonly affect adults over 45 years of age, but type one diabetes and type two diabetes are increasingly affecting younger people [16]. Factors contributing to normalisation of plasma sugar levels include, of course, adequate physical

activity and a good diet, but if diabetes or pre-diabetes is diagnosed, pharmacotherapy may need to be introduced according to specialist advice.

Result	Hemoglobin A1c level, %	Fasting plasma glucose level, mg/dL	2-h Plasma glucose from oral glucose tolerance test, mg/dL
Normal	<5.7	<100	<140
Prediabetes	5.7–6.4	100–125	140–199
Diabetes	≥6.5	≥126	≥200

3 Methods and Ranges of Diabetes Diagnosis Source: MeBushnell C, Kernan WN, Sharrief AZ, Chaturvedi S, Cole JW, Cornwell WK 3rd, Cosby-Gaither C, Doyle S, Goldstein LB, Lennon O, Levine DA, Love M, Miller E, Nguyen-Huynh M, Rasmussen-Winkler J, Rexrode KM, Rosendale N, Sarma S, Shimbo D, Simpkins AN, Sp

In type one diabetes the mainstay of therapy is insulin[18]. Drugs used to control glycaemia in type 2 diabetes before insulin therapy is implemented are metformin, which is associated with a significant reduction in the incidence of type 2 diabetes, and thiazolidinediones and α-glucosidase drugs which also reduce the risk of diabetes [17]. GLP-1 analogues are also gaining popularity. Semaglutide was more effective than placebo in reducing the risk of stroke in patients with type 2 diabetes in a clinical trial. Event rate 1.6% vs. 2.7%; HR, 0.61 [95% CI, 0.38-0.99]; P=0.04 [19].

Studies indicate that for every 1 % increase in haemoglobin A1c, the risk of stroke increases by 12 % [20], but maintaining haemoglobin A1c ≤ 6.5 % has no beneficial effect in preventing stroke [1].

Body weight

As mentioned in introduction overweight is a factor that has increased its contribution to stroke risk in recent years.

The BMI result will allow us to classify the patient into one of 3 classes of obesity;

- **Class I: BMI: 30.0-34.9 kg/m^2**
- **Class II: BMI: 35.0-35.9 kg/m^2**
- **Class III: BMI: ≥40 kg/m^2**

The BMI informs us about the risk of stroke accident. Every 5 unit increase in Body Mass Index score is associated with a 10 % increase in the risk of stroke [21]. This helps identify high-risk patients and implement appropriate management to prevent and reduce risk. Treatment of obesity may be based on a change in eating habits or increased physical activity, but often pharmacotherapy or surgical treatment is necessary.

The challenge, however, is to diagnose the patient correctly. The popular Body Mass Index has its limitations. For example, it does not take into account the increased proportion of muscular tissue in the patient's total weight, which will affect the final result of the index [1].

There are some different measurement methods that helps to objectify the diagnosis and also carries measurable information about cardio-vascular or stroke risk.

- **Waist circumference (WC) measured at midpoint between lower margin of the least palpable rib and top of the iliac crest [1]**
    - **Men**
        - **> 94 cm; increased cardiometabolic risk [22]**
    - **Women**
        - **>80 cm; increased cardiometabolic risk [22]**

Moreover, for each 10 cm more relative risk of stroke increases by 10% [23]

- **Waist to hip ratio (WHR) measured as WC/hip circumference measured around the widest portion of the buttocks [1]**
    - **Men**
        - **>0.90; increased cardiometabolic risk [22]**
    - **Women**
        - **>0.85; increased cardiometabolic risk [22]**

Moreover 0.1 unit increase in WHR corresponds to 16% increase in stroke risk [23]

Blood lipids

The effect of lipid disorders on stroke risk is not fully understood. It has been determined that increased total cholesterol increases the risk of stroke, whereas HDL cholesterol appears to have a stroke risk-reducing effect [13].

Monitoring cholesterol levels is an important factor in reducing the risk of stroke.

For individuals at very-high risk, whether in primary or secondary prevention, the therapeutic goal is to achieve a reduction in LDL-C by at least 50% from baseline, with an LDL-C target of less than 1.4 mmol/L (less than 55 mg/dL). If the patient is not currently using statins, this will likely require high-intensity LDL-lowering therapy. For those already on LDL-lowering

treatment, an increase in treatment intensity is necessary. For those at high risk, the goal is also to achieve a reduction in LDL-C by at least 50% from baseline, with an LDL-C target of less than 1.8 mmol/L (less than 70 mg/dL). For individuals at moderate risk, the LDL-C target is less than 2.6 mmol/L (less than 100 mg/dL). For those at low risk, the LDL-C target is less than 3.0 mmol/L (less than 116 mg/dL) [26].

For individuals at very-high risk, the secondary goal for non-HDL cholesterol is to keep it below 2.2 mmol/L (85 mg/dL). For those at high risk, the target is to maintain non-HDL cholesterol levels under 2.6 mmol/L (100 mg/dL). For people at moderate risk, the aim is to have non-HDL cholesterol below 3.4 mmol/L (130 mg/dL) [26].

Statins are used for this purpose, as they lower cholesterol levels, thereby reducing the risk of stroke [13]. In the past, some studies indicated an increased risk of bleeding during statin therapy. However, it is now believed that statins seem to reduce the risk of total and ischemic stroke without a significant increase in the risk of haemorrhagic stroke [24, 25].

Blood pressure (BP)

Hypertension is defined based on repeated office Systolic BP (SBP) values 140 mmHg and/or Diastolic BP (DBP) 90 mmHg. Hypertension is classified into grades based on the BP [40] [Table below].

Category	Systolic (mmHg)		Diastolic (mmHg)
Optimal	<120	and	<80
Normal	120-129	and	80-84
High normal	130-139	and/or	85-89
Grade 1 hypertension	140-159	and/or	90-99
Grade 2 hypertension	160-179	and/or	100-109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension	≥140	and	<90
Isolated diastolic hypertension	<140	and	≥90

4 Classification of office BP and definitions of hypertension grades [40].

The National Health Fund of Poland reported that in 2020 there were 9.9 million adults with hypertension in Poland, who accounted for 31.5 % of the adult population. This shows how massive part of our population is affected by this disease.

Strong, continuous, and progressive association between BP (especially SBP) and risk of ischemic and haemorrhagic stroke is documented by many cohort and electronic records linkage studies [37, 38]. High BP is also associated with other CVD complications and CVD risk can wary >30-fold at any level of BP [39].

To prevent stroke in adults with stage 2 hypertension or stage 1 hypertension with a higher risk of atherosclerotic CVD, lifestyle improvements and treatment with antihypertensive drugs are recommended to lower systolic/diastolic blood pressure (SBP/DBP) to below 130/80 mm Hg [1, 42-45]. Thiazide and thiazide like diuretics, calcium channel blockers, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are recommended as initial antihypertensive drug therapies [1, 46, 47] The latest ESH (European Society of Hypertension) guidelines recommend the use of 2 or more antihypertensive drugs from the start of hypertension therapy to achieve recommended blood pressure values [40].

Screening for hypertension in adults is essential to identify individuals eligible for treatment and at higher risk of stroke [1, 41]. There is a cardiovascular disease prevention programme in primary care in Poland, which an increasing number of facilities are joining. [https://www.gov.pl/web/zdrowie/narodowy-program-chorob-ukladu-krazenia2]

Nicotine exposure

Smoking is associated with a significant increase in stroke risk and is strongly correlated with the number of cigarettes smoked and duration of smoking. Active smokers have a 2.6 higher chance of stroke than non-smokers [48], while the level of risk falls back to population risk as early as 2-4 years after smoking cessation [13], which is a good predictor and draws attention to the relevance and effectiveness of smoking education and control.

Avoiding passive smoking is also an important factor, as its effects are similar to those of active smoking. It is estimated that about 1% of smoking-related deaths are in people who were not active smokers, but were exposed to second-hand smoke [49].

Sleep

Sleep disorders are currently attracting increasing interest among researchers as potential risk factors for stroke. Most studies focus on disorders related to apnoea during sleep.

Obstructive sleep apnoea (OSA) could be called another disease of affluence as it is closely related to the prevalence of obesity [27]. In middle-aged population in North America almost 30% of men and 15% women suffers from OSA [27]. OSA can be characterized by recurrent episodes of apnoea or hypopnea caused by obstruction of the upper airway during sleep [28]

and was not only classified as an independent risk factor for stroke [29, 30] but also have indirect effect on hypertension [31]. There are studies suggesting that continuous positive airway pressure (CPAP) as a treatment for OSA might reduce the risk of stroke [32, 33, 34], however direct evidence of this effect is lacking and there is need for further research in that matter.

Unfortunately, there are still few studies focusing on other sleep disorders in stroke prevention. In one prospective study, long sleep duration was associated with increased risk of total and ischemic stroke [35] and analysis of The INTERSTROKE study showed that sleep disturbance symptoms were common and associated with a graded increased risk of stroke [36]. It remains unclear whether these symptoms represent individual factor or present as the marker of increased individual risk [36].

One thing is certainly clear – the relationship between sleep disorders and stroke needs further attention and may provide new targets for stroke prevention research.

Summary

Correct identification of risk factors is part of the American Heart Association's strategy to prevent the onset of cardiovascular disease, as this has better outcomes than treating diseases that have already occurred [10]. A review of the available literature has shown that 90 % of modifiable risk factors are responsible for the occurrence of such a serious disease as stroke. The categories identified in the recommendations are objective and measurable and improvements in individual parameters bring tangible benefits in the form of significant reductions in stroke incidents and their complications. The vast majority of health-promoting actions can be performed by the patient and translate directly into health and quality of life. Education of the public plays a very important role.

Primary health care plays an extremely important role as the first point of contact between the patient and the health care system and by virtue of providing regular care for the patient. Health education and prevention and screening programmes should be increasingly widespread and primary prevention should come to the forefront in planning community health strategies/policies.

Disclosure

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Writing - Review and Editing: Borys Bondos [BB], Robert Kochan [RK], Kacper Lee [KL]

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