RISK ASSESSMENT IN PUBLIC HEALTHCARE

STROKE AND STROKE RISK FACTORS AS DISEASE BURDEN

S. Ozturk

Selcuk University, Faculty of Medicine, Selcuklu-Konya, 42130, Turkey

Stroke is the most common cause of disability and death in the world. Cardiovascular disease rates increase with age (10.9 % for people aged 20–30 years and 85.3 % for people older than 80 years). Coronary heart diseases is the leading cause of deaths attributable to cardiovascular diseases in the United States, followed by stroke, high BP, HF, diseases of the arteries, and other cardiovascular diseases. The report on the global burden of neurological disorders has shown that hemorrhagic stroke accounted for 35.7 % in it, and ischemic stroke, 22.4 %. Seven indicators are important and strategic to prevent cardiovascular disorders; they include healthy diet, sufficient physical activity, smokingstatius, BMI, cholesterol level, blood pressure, and glucose in blood on a fasting stomach. These indicators are associated with healthy behavior (diet quality, PA, smoking, BMI) which are as important as health factors (blood cholesterol, BP, blood glucose). There is a strong protective association between ideal cardiovascular health indicators and many clinical and preclinical conditions including premature all-cause mortality, stroke, CVD mortality, ischemic heart disease mortality, HF, deep venous thromboembolism, and pulmonary embolism. Atrial fibrillation, metabolic syndrome, renal failure, and sleep apnea are important risk factors which are modifiable and treatable. Air pollution has been reported as an increasing and very important risk factor for stroke. COVID-19 has been reported as another new stroke risk factor during the pandemic. Future targets must include each cardiovascular health indicator to decrease stroke risk burden and stroke risk.

Key words: stroke, cardiovascular diseases, health indicators, risk factors, disease burden.

Neurological diseases account for 10.2 % of global loss in health, cause 16.8 % of global deaths, and 9.4 million people in the world lose their lives every year because of neurologic diseases. Stroke is the most common cause of disability. The striking facts show that every 40 seconds someone in the United States has a stroke and someone dies of one approximately every 4 minutes.

Stroke death rate decreases with the improvement in acute stroke treatment and widely usage of stroke units. According to the AHA statistics (2018) the 10 leading causes of death are heart disease (No. 1), cancer (No. 2), chronic lower respiratory diseases (No. 3), unintentional injuries (No. 4), stroke (No. 5), Alzheimer disease (No. 6), Diabetes Mellitus (No. 7), influenza and pneumonia (No. 8), kidney disease (No. 9), suicide (No. 10). There is also an important changes in ICD 11 (stroke listed under the brain disorders) and this important step may support more accurate statistics for stroke prevalence and incidence [1].

High body mass index, high fasting plasma glucose, and smoking are the first, second, and third leading years lived with disability and injury risk factors in the United States in both 1990 and 2019, whereas smoking dropped from first to third leading years lived with disability and injury risk factor during this time period. Smoking and high systolic BP remained the first and second leading years of life lost risk factors in the United States in both 1990 and 2019. High systolic BP and smoking are the first and second leading years of life lost risk factors

---

Serefnur Ozturk – Doctor of Medical Sciences, Professor of Neurology, Fellow of European Academy of Neurology (EAN) (e-mail: serefnur@yahoo.com; tel.: 0 (332) 241 00 41).

globally in 2019. High fasting plasma glucose and high body mass index were the first and second leading years lived with disability and injury risk factors globally in 2019. The recent data show that cardiovascular disease rates increase with age (10.9 % for 20–30 ages and 85.3 % for older 80 ages). Coronary hearth diseases (43.8 %) is the leading cause of deaths attributable to cardiovascular diseases in the United States, followed by stroke (16.8 %), high BP (9.4 %), HF (9.0 %), diseases of the arteries (3.1 %), and other cardiovascular diseases (17.9 %).

Between 1990 and 2010, ischemic stroke mortality decreased 37 % in high-income countries and 14 % in low and middle-income countries. Hemorrhagic stroke mortality decreased 38 % in high-income countries and 23 % in low- and middle-income countries. The report on the global burden of neurological disorders showed that burden consists of 35.7 % hemorrhagic stroke, 22.4 % ischemic stroke, 12.7 % migraine, 9.9 % epilepsy, 6.4 % dementias, 1.1 % Parkinson diseases, 1.0 % tension headache other 10.2 % [2–5].

Risk Factors for Stroke. AHA-Health Metrics were defined to follow health risk and management of this parameters. Seven Health Metrics which are important and strategic to prevent cardiovascular disorders; Healthy diet pattern, sufficient physical activity, smoking, BMI, cholesterol level, blood pressure, fasting blood glucose. These metrics include also health behaviours (diet quality, PA, smoking, BMI) which are as important as health factors (blood cholesterol, BP, blood glucose).

There are strong protective association between ideal cardiovascular health metrics and many clinical and preclinical conditions including premature all-cause mortality, stroke, CVD mortality, ischemic heart disease mortality, HF, carotid arterial wall stiffness, coronary artery calcium progression, impaired physical function, cognitive decline, depression, end-stage renal disease, chronic obstructive pulmonary disease, deep venous thromboembolism, and pulmonary embolism [5].

High blood pressure. It was reported that there are 3.47 billion adults worldwide with systolic BP of 110 to 115 mmHg or higher in 2015. The death rate attributable to high BP increased by 10.5 %, and the actual number of deaths attributable to high BP rose by 37.5 % from 2005 to 2015.

Smoking and tobacco use. According to the AHA statistics, the prevalence of current smoking in the United States in 2015 was 15.1 % for adults and 4.2 % for adolescents. Despite all efforts to reduce, tobacco use remains the leading cause of preventable death in the United States and globally. It was estimated to account for 7.2 million deaths worldwide in 2015. Recently, there has been a rapid increase in e-cigarette use especially among adolescents. Cigarette smoking is known as an independent risk factor for both ischemic stroke and SAH. Current smokers have a 2 to 4 times increased risk of stroke compared with nonsmokers or those who have quit for > 10 years lowering CVD risk. Another ignored risk factor is secondhand smoke which is as harmful as smoking. Nonsmokers who are exposed to secondhand smoke at home or at work increase their risk of developing CHD by 25 % to 30 %. Exposure to secondhand smoke; increases the risk of stroke by 20 % to 30 %, associated with increased mortality after a stroke.

Physical inactivity. Physical inactivity is the fourth-leading risk factor for global death, responsible for 1 to 2 million deaths annually. It was reported that only 21.5 % of American adults achieve adequate leisure-time aerobic and muscle-strengthening activities to meet the physical activity guidelines. The prevalence of adolescents meeting the aerobic physical activity guidelines is 27.1 %.

Nutrition. Nutrition has been reported as a leading risk factor for stroke and other cardiovascular disorders. 45.4 % of US deaths caused by heart disease, stroke, and type 2 diabetes mellitus (DM) (cardiometabolic mortality) were attributable to poor dietary habits.

The top contributing poor dietary factors were reported as; High sodium intake, low levels of nuts and seeds, high intake of processed meats, low consumption of seafood omega-3 fats, low intake of vegetables, low intake of

fruits, and high consumption of sugar-sweetened beverages [6].

Obesity and overweight. Obesity is a very common health problem in the world. It has been reached a very risky level for every ages including children. There are important results from a meta-analysis from 2016 which suggests that CVD risk was higher (relative risk, 1.45) in obese individuals without metabolic syndrome than in metabolically healthy normal-weight participants, which suggests that obesity is a risk factor even in the absence of high blood pressure, high cholesterol, and DM [3].

High blood cholesterol and other lipids. An estimated 28.5 million adults ≥ 20 years of age have serum total cholesterol levels ≥ 240 mg/dL, with a prevalence of 11.9 %. 21 % of youths 6 to 19 years of age have at least 1 abnormal cholesterol measure. 56.0 million (48.6 %) US adults ≥ 40 years of age are eligible for statin therapy based on the 2013 American College of Cardiology / AHA guidelines [7].

Diabetes mellitus. Diabetes mellitus rate increases with the increase of obesity, unhealthy diet. In 2015, an estimated 5.2 million deaths globally were attributed to DM. The prevalence of diagnosed DM was estimated to range from 5.6 % to 20.4 %, and the prevalence of undiagnosed DM ranged from 3.2 % to 6.8 %.

Atrial fibrillation. Atrial fibrillation is an increasing risk factor with age. Multiple lines of evidence have increased awareness of the burden of unrecognized AF. In individuals without a history of AF with recent pacemaker or defibrillator implantation, subclinical atrial tachyarrhythmias were detected in 10.1 % of patients.

Subclinical atrial tachyarrhythmias were associated with a 5.6-fold higher risk of clinical AF and ≈ 13 % of ischemic strokes or embolism.

Sleep apnea. A modifiable risk factor sleep apnea must be taken into consideration. The prevalence of sleep-disordered breathing, defined as an AHI ≥ 5, has been estimated to be 34 % for men and 17 % for women aged 30 to 70 years. Obstructive sleep apnea causes increase in stroke especially in men [8].

Metabolic syndrome. The prevalence of metabolic syndrome was 17 % among people < 40 years old, 29.7 % for people 40 to 49 years old, 37.5 % among those 50 to 59 years old, and > 44 % among people ≥ 60 years of age.

The prevalence of metabolic syndrome was higher among females (34.4 %) than males (29 %) and increased with advancing age.

Of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks analysed in GBD 2013. It was assessed risk–outcome pairs (17 risks and stroke-related DALYs) that met explicit evidence criteria for 188 countries [9].

Top risk factors ranked by number of DALYs attributable to stroke for both sexes combined in 21 regions in 2013 DALY= disability-adjusted life-year (Figure 1) [10–12].
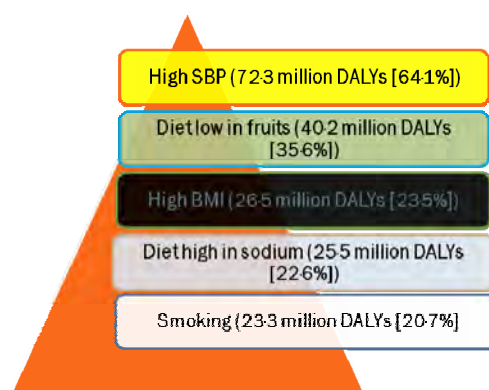

Figure 1. The five leading risk factors for DALYs
(GBD 2016 – Feigin et al. [13])

Air pollution. A new and very important risk factors were environmental factors (air pollution and lead exposure; 33.4 %, 95 % CI 32.4−34.3) were the second and third largest contributors to DALYs [14].

Globally, 29.2 % (95 % CI 28.2–29.6) of the burden of stroke was attributed to air pollution. It has been reported that air pollution has emerged as a significant contributor to global stroke burden, especially in low income and middle-income countries, and therefore reducing exposure to air pollution should be one of the main priorities to reduce stroke burden in these countries.

Eating habits and life styles change with the change of demographics and economic levels. Globally, there were a significant increase in the stroke-related DALYs associated with high BMI low physical activity, high fasting plasma glucose high SBP, diet high in sugar-sweetened beverages, high total cholesterol, ambient particulate matter pollution of aerodynamic diameter less than 2.5 μm ($PM_{2.5}$), alcohol use, diet high in sodium, diet low in vegetables, and smoking. It can be concluded that if these trends continue the differences will be increase as dependent of countries income levels. Especially diet high in sodium is an important marker which is able to affect other risk factors [6, 14].

A promising result is a reality which shows that more than 90 % of the stroke burden is attributable to modifiable risk factors, and achieving control of behavioural and metabolic risk factors could avert more than three-quarters of the global stroke burden.
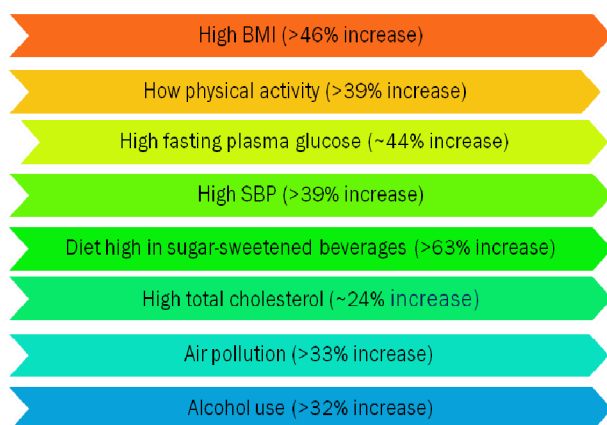

Figure 2. Increase in the stroke-related DALYs and risk factors (1990–2013) (GBD 2016 – Feigin et al. [13])

The COVID-19 pandemic is an additional ongoing threat for this widespread and important group of diseases. While the field is rapidly emerging, our current knowledge on the role of COVID-19 in stroke is increasing. Evidence suggests that infected patients may develop significant coagulopathy which leads to thromboembolic complications like stroke, peripheral artery thrombosis, deep vein thrombosis, pulmonary embolism, myocardial in-farction, ischemic stroke, and venous sinus thrombosis. Histopathologic analysis of the ischemic brain of a COVID-19 patient revealed hypoxic neurons, significant edema from the underlying ischemic insult, fibrin thrombi in small vessels, and fibroid necrosis of the vascular wall without any signs of vasculature inflammation. The authors suggested that the cerebrovascular thromboembolic events in COVID-19 infection may be related to acquired hypercoagulability and coagulation cascade activation due to the release of inflammatory markers and cytokines, rather than virus-induced vasculitis. Microthrombi within the vessels were more consistent with a systemic inflammatory response-mediated mechanism, probably related to elevated serum inflammatory markers such as D-dimer and fibrinogen [15, 16].

Lockdown periods can cause a hesitation among patients to admit themselves to hospitals for routine care of chronic diseases, or for acute health care such as stroke, which is a time-dependent condition and irregularity for routine checkups for risk factor prevention.

To prevent these proven risk factors and to decrease burden of stroke ESO published an action plan for 2030 [17]. To reduce effect of stroke in public health and to increase supports by health authorities and politicians, this was an important strategy. General targets and item specific targets were defined. General target for 2030 was defined to reduce the absolute number of strokes in Europe by 10 % and to treat 90 % or more of all patients with stroke in Europe in a dedicated stroke unit as the first level of care. The national awareness and action was important and national societies were motivated to have national plans for stroke encompassing the entire chain of care from primary prevention to life after stroke.

Targets for primary prevention. Achieving universal access in Europe to primary preventive treatments based on improved and more personalised risk prediction, having blood pressure detected and controlled in 80 % of persons with hypertension.

Secondary prevention: The statistical data show that secondary prevention as important

as primary prevention to reduce stroke burden. Secondary preventionIncluding secondary prevention in national stroke plans with follow-up in primary / community care, ensuring that at least 90 % of the stroke population is seen by a stroke specialist and have access to secondary prevention management (investigation and treatment), ensuring access to key preventative strategies: lifestyle advice, anti-hypertensives, lipid lowering agents, antiplatelets, anticoagulants, oral hypoglycaemic agents and insulin, carotid endarterectomy, and PFO closure.

Conflict of interests. The authors declare there is no any conflict of interests.

References

1. Virani S.S., Alonso A., Aparicio H.J., Benjamin E.J., Bittencourt M.S., Callaway C.W., Carson A.P., Chamberlain A.M. [et al.]. Heart Disease and Stroke Statistics – 2021 Update: A Report From the American Heart Association. *Circulation*, 2021, vol. 14, no. 8, pp. e254–e743. DOI: 10.1161/CIR.0000000000000950

2. Chin J.H., Vora N. The global burden of neurologic diseases. *Neurology*, 2014, vol. 83, no. 4, pp. 349–351. DOI: 10.1212/WNL.0000000000000610

3. Mills K.T., Bundy J.D., Kelly T.N., Reed J.E., Kearney P.M., Reynolds K., Chen J., He J. Global Disparities of Hypertension Prevalence and Control: A Systematic Analysis of Population-Based Studies From 90 Countries. *Circulation*, 2016, vol. 134, no. 6, pp. 441–500. DOI: 10.1161/CIRCULATIONAHA.115.018912

4. GBD 2015 Tobacco Collaborators. Smoking prevalence and attributable disease burden in 195 countries and territories, 1990–2015: a systematic analysis from the Global Burden of Disease Study 2015. *Lancet*, 2017, vol. 389, no. 10082, pp. 1885–1906. DOI: 10.1016/S0140-6736(17)30819-X

5. Global Health Risks: Mortality and Burden of Disease Attributable to Selected Major Risks. Geneva, Switzerland, World Health Organization, 2009, 63 p.

6. Powles J., Fahimi S., Micha R., Khatibzadeh S., Shi P., Ezzati M., Engell R.E., Lim S.S. [et al.]. Global, regional and national sodium intakes in 1990 and 2010: a systematic analysis of 24 h urinary sodium excretion and dietary surveys worldwide. *BMJ Open*, 2013, vol. 3, no. 12, pp. e003733. DOI: 10.1136/bmjopen-2013-003733

7. My Life Check. Life's Simple 7. *American Heart Association*. Available at: https://www.heart.org/en/healthy-living/healthy-lifestyle/my-life-check--lifes-simple-7 (26.04.2021).

8. Molnar M.Z., Mucsi I., Novak M., Szabo Z., Freire A.X., Huch K.M., Arah O.A., Ma J.Z. [et al.]. Association of incident obstructive sleep apnoea with outcomes in a large cohort of US veterans. *Thorax*, 2015, vol. 70, no. 9, pp. 888–895. DOI: 10.1136/thoraxjnl-2015-206970

9. GBD 2013 Risk Factors Collaborators, Forouzanfar M.H., Alexander L., Anderson H.R., Bachman V.F., Biryukov S., Brauer M., Burnett R. [et al.]. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*, 2015, vol. 386, no. 10010, pp. 2287–2323. DOI: 10.1016/S0140-6736(15)00128-2

10. Global Status Report on Noncommunicable Diseases 2014. *WHO*, 2014. Available at: http://apps.who.int/iris/bitstream/handle/10665/148114/9789241564854_eng.pdf?sequence=1 (26.04.2021).

11. Neurological Disorders Collaborator Group. Global, regional, and national burden of neurological disorders during 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet Neurol.*, 2017, vol. 16, no. 11, pp. 877–897. DOI: 10.1016/S1474-4422(17)30299-5

12. Thrift A.G., Howard G., Cadilhac D.A., Howard V.J., Rothwell P.M., Thayabaranathan T., Feigin V.L., Norrving B., Donnan G.A. Global stroke statistics: An update of mortality data from countries using a broad code of "cerebrovascular diseases". *Int. J. Stroke*, 2017, vol. 12, no. 8, pp. 796–801. DOI: 10.1177/1747493017730782

13. Feigin V.L., Norrving B., Mensah G.A. Global Burden of Stroke. *Circ. Res.*, 2017, vol. 120, no. 3, pp. 439–448. DOI: 10.1161/CIRCRESAHA.116.308413

14. Roth G.A., Johnson C., Abajobir A., Abd-Allah F., Abera S.F., Abyu G., Ahmed M., Aksut B. [et al.]. Global, Regional, and National Burden of Cardiovascular Diseases for 10 Causes, 1990 to 2015. *J. Am. Coll. Cardiol.*, 2017, vol. 70, no. 1, pp. 1–25. DOI: 10.1016/j.jacc.2017.04.052

15. Mondal S., Quintili A.L., Karamchandani K., Bose S. Thromboembolic disease in COVID-19 patients: A brief narrative review. *J. Intensive Care*, 2020, vol. 8, pp. 70. DOI: 10.1186/s40560-020-00483-y

16. Federico A. Brain Awareness Week, COVID-19 infection and Neurological Sciences. *Neurol. Sci.*, 2020, vol. 41, no. 4, pp. 747–748. DOI: 10.1007/s10072-020-04338-0

17. Norrving B., Barrick J., Davalos A., Dichgans M., Cordonnier C., Guekht A., Kutluk K., Mikulik R. [et al.]. Action Plan for Stroke in Europe 2018–2030. *European Stroke Journal*, 2018, vol. 3, no. 4, pp. 309–336. DOI: 10.1177/2396987318808719