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Overview

Epidemiology of stroke

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Abstract

The epidemiology of stroke may be changing over time as a result of a number of factors, including an aging population and advances in the prevention and treatment of stroke. Epidemiological indicators and research of stroke have great significance in estimating the impact of this disease on the population. Such research states the distribution of this illness and factors by which it is influenced, follows short-term and long-term consequences, as well as socio-economic burden of stroke for the whole community.

Data on stroke prevalence is important for creating the right strategies for health care in a specific area. Stroke-related mortality in any population is dependent upon three main factors: the incidence of stroke in the population, quality of medical care available, and the prevalence of cardiovascular diseases and comorbidities that can affect the likelihood of surviving stroke events. The quality of medical care available influences both the number of individuals suffering from stroke and the proportion of case-fatality among them.

Epidemiological data shows that stroke is one of the leading causes of death and long-term disability in most industrialized populations, and the same is true for Croatia. The existing system of health care for stroke patients does not meet the needs and is not in accordance with latest trends in developed countries. Hence, there is a need for its reorganization and design of the national project for stroke prevention and treatment similar to those in European countries with favorable epidemiological data.

INTRODUCTION

Stroke is one of the largest health burdens in most industrialized populations, as well as in Croatia. The epidemiology of stroke may be changing over time as a result of a number of factors, including an aging population and advances in the prevention and treatment of stroke. Given the observed changes in the epidemiology of stroke over time, it is important to obtain a good overview of the most recent data. Epidemiological indicators and results of neuroepidemiological research of stroke and other cerebrovascular diseases have great significance in estimating the scope of the problem of stroke in the population. Such research states the distribution of this illness and factors by which it is influenced, follows short-term and long-term consequences, as well as socio-economic burden of stroke for the whole community. Epidemiological trials usually include hospital material, but population trials provide the most accurate epidemiological data. Whereas population trials are important for stating morbidity (incidence and prevalence), mortality, long-term outcome and life quality after stroke, clinical epidemiological trials enable estimation of case fatality and short-term outcome of this disease.

Neuroepidemiological research encounters many methodological problems. Population research depends on specific knowledge and willingness of participants in the research. Although the most reliable data include deceased who died in hospitals, not even they are completely accurate, unless they are confirmed by an autopsy. Test results of a coroner are even less accurate. Some cases of stroke do not have to manifest themselves in classic signs, such as motor paralysis and speech problems, which causes difficulties in diagnosis. It is hard to make a diagnosis on people who died suddenly outside the hospital, due to more difficult differentiation of cardiovascular, cerebrovascular and other causes of death. Apoplectic syndrome can be caused by other factors, such as decompensated brain tumors or other acute disorders of the central nervous system *(1)*.

Modern research of neurological diseases in Croatia started at the end of 1960's and in the early 1970's. Pursuant to the instructions of World Health Organization (WHO), a group of experts performed systematic epidemiological research in the Centre for Cerebrovascular Diseases »Trnje« in Zagreb. The first symposium on cerebrovascular diseases was held in Zagreb in 1971. On the second symposium, which was held in 1974 with participation of experts from WHO, one of the main topics was epidemiology of cerebrovascular diseases (CVD). Methodologies of many specific subjects, important for diagnostics and therapy of these diseases, had epidemiological characteristics. In that way modern concept of treating CVD started to form: prevention, early diagnosis and urgent treatment, as well as directed neuroepidemiological research of problems in this area *(2)*.

DEFINITION AND CLASSIFICATION

WHO defines stroke as »rapid development of clinical signs of focal (or global) brain function disorders, with symptoms which last 24 hours or longer or lead to death, without other clear cause, except signs of blood vessel damage« *(3)*. This disease is classified into two main types: brain ischemia due to thrombosis, embolism or systemic hypoperfusion and brain hemorrhage due to intracerebral or subarachnoidal hemorrhage. 80 % of strokes are caused by ischemia and the rest by hemorrhage. Two main categories of this disease are diametrically opposite: hemorrhage is characterized by an excessive amount of blood inside the closed intracranial cavity, whereas ischemia is characterized by lack of blood and inadequate amount of oxygen and nutrients in a specific part of brain. Each of these categories can be divided into subtypes, which have different causes, clinical manifestations, clinical course, outcome and therapeutic strategies.

There are different approaches to classification of acute stroke. International classification of diseases and problems made by the WHO regarding health (tenth audit--ICD 10) includes diseases and signs, symptoms, abnormal test results, complaints, social circumstances and external causes of injuries and illnesses. This classification classifies stroke under codes from I 60 to I 69 into following subgroups: subarachnoidal hemorrhage, intracerebral hemorrhage, other non-traumatic hemorrhages, cerebral infarct caused by extracerebral or intracerebral occlusion, as well as non-specific stroke *(4)*.

Classification of Oxford Community Stroke project is primarily based on initial symptoms; episodes of stroke are classified based on development of symptoms such as: primary intracerebral hemorrhage, total anterior circulation syndrome, partial anterior circulation syndrome, lacunar circulation syndrome and posterior circulation syndrome. These five entities anticipate the development of stroke, part of brain which was compromised, the main cause behind the incident and disease prognosis *(5, 6)*. TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification of ischemic stroke is very practical and is based on clinical symptoms, as well as on results of further research. Based on that, stroke is classified as a consequence of: thrombosis or embolism due to atherosclerosis of large blood vessels; embolism which started in the heart; occlusion of small blood vessels; other stated causes; undetermined causes (two possible causes, one unidentified cause or incomplete research) *(7)*.

Classical definition of transitory ischemic attack (TIA) is a sudden start of focal neurological symptom and/or sign, which lasts less than 24 hours and probably is caused by temporary reduced bloodstream, which leads to brain ischemia in the area, which produces symptoms. Recovery period of blood stream is enough to make ischemia temporary and to avoid infarction. Nevertheless, arbitrary nature of 24-hour time limit and lack of specific pathophysiological significance reduces clinical and research usefulness of the TIA term. Recognition of these terms led to evolution in a definition and that process was supported by improvements in neuroimaging, especially by imaging measured by diffusion, which enables very early identification of ischemic brain damage. Infarction usually develops when focal temporary neurological symptoms last more than one hour. So the benign connotation of the term »TIA« is changed by cognition that even small ischemia can cause permanent brain damage. Based on facts stated in the past years, redefining of criteria is suggested, according to which TIA would include neurological symptoms, which last less than an hour without image evidence on ischemia of brain tissue, and ischemic stroke includes neurological symptoms, which last more than an hour and/or when there are imaging evidence of brain tissue damage *(8)*.

NEUROEPIDEMIOLOGICAL DATA

Incidence

Well performed trials on stroke incidence include usage of standard definition, which was provided by WHO, prospective studies on a large, well defined and representative sample, as well as comprehensive and understandable methodology of detecting the ill and identifying non-fatal cases treated outside the hospital and those who died soon after the illness started. Stroke incidence, strictly speaking, would refer to incidents which appear

for the first time in life of a person (first-ever stroke), but some trials include also recurrent strokes. It is estimated that approximately 4 million people suffer from stroke annually. Out of that number, approximately 570 000 cases occur in Europe and approximately 500 000 in United States of America. Age-standardised incidence rates are usually used in stroke incidence reviews. International epidemiological trials show that rates grow exponentially with age, from 0.3‰ in the third and fourth decade of life, all the way to 30‰ in the eighth and ninth decade of life, which makes an average of 1–2‰. Recent data shows that the incidence of stroke in France is 114 cases per 100 000 persons per year, in Germany 350, in Italy 223, in Spain 141–220, and in UK 161 *(9)*. In 2005 a multicentric trial of incidence of stroke and transitory ischemic attacks was implemented with the aim of determining real incidence rates of acute cerebrovascular diseases in Republic of Croatia (RC). The research used internationally accepted methodology and was performed during one year period from January 1st till December 31st, 2005. All cases of stroke and TIA were carefully recorded in cooperation with primary care physicians. Multicentric trial included population of 89 501 people of all age in four macroregional centres of RC (Osijek-Slavonski Brod, Split, Rijeka and Zagreb). Stroke incidence rate for the entire area of RC amounted to 251/100 000. In individual regional centres the following stroke incidence rates were noted: Osijek-Slavonski Brod 302/100 000, Zagreb 290/100 000, Rijeka 220/100 000, Split 196/100 000. TIA incidence rate for the entire area of RC amounted to 101/100 000. In individual regional centres the following TIA incidence rates were noted: Osijek-Slavonski Brod 157/100 000, Zagreb 87/100 000, Rijeka 90/100 000, Split 22/100 000. In the continental part of the RC (Osijek-Slavonski Brod, Zagreb) Stroke incidence rate amounted to 298/100 000, and TIA incidence rate amounted to 130/100 000. In the coastal part of the RC (Split, Rijeka) stroke incidence rate amounted to 205/100 000, and TIA incidence rate amounted to 49/100 000. Stroke incidence was 1.45 times bigger, and TIA incidence was 2.64 times bigger in the continental part than in the coastal part of the RC. The trial revealed relatively high incidence rates of acute CVD (stroke and TIA) in the RC, which confirmed that CVDs are a large public health problem. Significantly higher incidence rates in the continental part of the country than in the coastal area showed that way of life and environment influence development of stroke and other cerebrovascular disorders *(10)*.

Prevalence

Data on stroke prevalence is the best indicator of how spread a disease is in a population and it also enables creating right strategies of health actions and total health care in a specific area. Stroke prevalence rates in the world vary between 5‰ and several percentages. Recent data show that the prevalence of stroke in Italy is 1.47%, in UK 1.7% and in US 2.6% *(9)*. Several years ago the population epidemiological trial was implemented in our country with the aim of determining prevalence of acute CVD: TIA and stroke in the Osijek-Baranya County. Internationally acknowledged work methodology for the population epidemiological trials, which was recommended by the WHO was used in this research. So-called door-to-door epidemiological research was implemented with a help of a questionnaire, which was designed by neurological experts experienced in stroke problems, and afterwards additional data control was performed in medical charts of people included in the trial, in cooperation with doctors of primary health care. The trial included population of 1423 people of all age. Prevalence of acute CVD was 3.30%, out of which 2.04% was stroke prevalence and 1.26% was TIA prevalence. In men, CVD prevalence amounted to 3.04%, out of which 1.88% was stroke and 1.16% was TIA. In women, CVD prevalence of 3.56% was recorded, out of which 2.19% was stroke and 1.37% was TIA. Prevalence of acute CVD is increasing progressively as the population gets older. In the age group 55–64 it amounted to 9.44% (stroke 6.67% and TIA 2.78%), in the age group 65–74 it amounted to 10.60% (stroke 6.82% and TIA 3.79%), and the highest prevalence was recorded in the age group 75–84 where it amounted to 14.86% (stroke 10.81% and TIA 4.05%). The trial has shown high prevalence rate of acute CVD in the Osijek-Baranya area and has confirmed that these diseases are one of the leading public health problems in Eastern Croatia *(11)*.

Mortality

Mortality related to stroke in any population is dependent upon three main factors: the incidence of stroke in the population, the quality of medical care available to individuals who have suffered a stroke and the prevalence of cardiovascular disease and comorbidities that can affect the likelihood of patients surviving stroke events. The quality of medical care available influences both the number of individuals suffering from stroke and the proportion of case-fatality among them. Worldwide, there are approximately 4.6 million deaths from stroke each year, and three quarters of these occur in developing countries. The estimate is based on death certificate data, which cover only about one third of the world's population, and extrapolation from total mortality rates. Despite their limitations, death certificate data show that in recent decades stroke death rates have declined dramatically, at least in industrial countries, with as much as a 7% per annum decline occurring in Japan since the mid-1970s *(12)*. In developing countries where death certificate information is available, the general trend is also downward. Not all countries have benefited, however. Countries in Eastern European region still register high stroke death rates. Mortality rates for stroke in Europe vary significantly. The highest rate of 249/100 000 was noted in Bulgaria, and the lowest of 27/100 000 in Switzerland. Recent data show that the age-standardised stroke-mortality rates in France are 24–38, in Germany 37–47, in Italy 41–68, in Spain 38–52, in UK 46–53 and in US 32–35 deaths per 100 000 persons per year *(9)*. East European countries have higher total mortality, whereas

the lowest rates were noted in Scandinavian countries, Switzerland and the Netherlands. Mortality rates were dramatically reduced in the past few decades in Japan and West European countries. In comparison, in East European countries there has been a constant increase in mortality rate caused by stroke in the same period, which continued in transition period of these countries.

Trials that show secular changes in mortality caused by some diseases, throughout a long period of years or decades, have a special significance. To analyse secondary trend of dying age, periodical and generation impacts should be taken into consideration. Secular trend of dying from stroke in the USA in the period 1900–1995 is shown by the following mortality rates per 100 000 inhabitants. The rate was 106.3 in 1900, 104 in 1950, followed by a decrease to 74.6 in 1980 and to 57.9 in 1990. After that, the trend of decreasing mortality rate stopped, and in 1995 the rate of 60.2 was noted. A significant trial on secular trends of dying from stroke in Croatia was conducted in the period of 30 years, from 1958 to 1997, and showed a constant trend of mortality increase from this disease during that period. Whereas total number of inhabitants increased by 14% during the observation period, number of deceased from stroke increased by 64%. Proportional mortality rate from CVD, for population 35–74 years of age, increased from 9% in 1958 to 14,9% in 1987, and standardized mortality rate from stroke for population 35–74 years of age increased from 118/100 000 to 191/100 000 inhabitants. Data analysis for the next ten years showed that secular trend of growth of total number of deceased and growth of proportional mortality rate from CVD had continued in a population 35–74 years of age. Mortality rates are especially high in the continental area, in cities Osijek and Varaždin, and they are, in some cases, 2–3 times higher than in coastal area *(13)*. If we compare age standardized mortality rates in Croatia and in Europe from the database of the WHO program »Health for Everybody«, the rate for cerebrovascular diseases for all ages in total amounted to 127.8 in 2004 for Croatia, and to 57.1 for the EU members before 2004 (2003 was the last available year), and 107.0/100 000 for the EU members since 2004. For age group 0–64, the rate in Croatia was 20.9, slightly lower than rate in »new« EU members (21.1), but almost 3 times higher than mortality rate in »old« EU members 7.6/100 000. *(14)*. The latest data showed that out of all deceased in Croatia in 2008, 9.6 percent died from stroke and its consequences, which was 6190 people. Mortality rate for stroke in 2008 was 182.0/100 000 (15).

Case fatality

Case fatality is a proportion of patients who suffered from stroke, and who died after a specific period after the illness occurred. It is usually expressed as a percentage of deceased in the 28-day period. Predicators that influence early mortality are: localisation and size of infarct and haemorrhage, degree of consciousness disorders, degree of neurological deficit, older age, male gender, diabetes, arterial hypertension, cardiac diseases, temperature, dysphagia, sphincter incontinence, etc. Fatal outcome of stroke is caused by central and peripheral complications. The most frequent central complications are: cerebral oedema, transtentorial herniation, hemorrhagic transformation of ischemia, epileptic seizures, depression. More frequently, the death of patients with stroke is caused by peripheral (systemic) complications: deep venous thrombosis and pulmonary embolism, bronchopneumonia, urinary infection, septicaemia, aspiration, cardiac arrhythmia, myocytolysis, uncontrolled hypotension, sudden death. It is estimated that approximately one third of people who suffered from stroke die, one third has severe and one third mild residual neurological deficit, or is without deficit. Factors which point out to poor outcome of stroke are: older age, male gender, presence of diabetes, arterial hypertension and cardiac disease, temperature, dysphagia, incontinence, loss of consciousness, severe neurological deficit, cognitive disorders, localisation and infarct size, oedema and moving of central structures, biochemical and haematological disorders, etc. Our research of short--term and long-term outcome of ischemic stroke showed that approximately one quarter of patients die in the first month and approximately one half in the next six months. Mortality in five-year period after ischemic stroke goes up to 60%. Among patients approximately 75% of cases are the first, and 25% of cases are recurrent strokes. Risk of recurrent stroke is the highest in the first year and is around 10 %, and every other year around 5 % *(16)*. The most important indicators for recurrent stroke are: type of stroke, earlier TIAs, arterial hypertension, heart valve disease, arterial fibrillation, congestive heart failure, high level of glucose in blood, male gender and alcohol abuse.

CONCLUSION

Epidemiological data shows that stroke is one of the leading causes of death and long-term disability in most industrialized populations, as well as in our country. Community-based studies are important for the assessment of morbidity (incidence and prevalence), mortality and long-term outcome of stroke. Hospital-based studies enable the assessment of case fatality and short-term outcome of stroke. In epidemiological researche of stroke it is necessary to use internationally accepted standards. Although results on stroke epidemiology in our country are outdated and incomplete, studies conducted on hospital material in the last two decades show the current state and point to negative trends in stroke incidence, prevalence and case fatality. The existing system of health care for stroke patients does not meet the needs and is not in accordance with latest trends in developed countries. Hence, there is a need for the reorganization of the health care system and design of the national project for stroke prevention and treatment similar to those in European countries with favourable epidemiological data. Croatian Association for Neurovascular Disorders of Croatian Medical Association and Croatian Association for Stroke Prevention created guidelines for modern approach to treatment and stroke prevention *(17)*. Also, implementation of National Project of Taking Care of

Patients with Stroke, which was created by the Ministry of Health of the Republic of Croatia, is underway. The final results of these activities should be reduced morbidity, mortality and case-fatality from stroke, prevented invalidity and incapability, improved life quality, as well as reduced social and economic burden of this decease on the whole community.

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