The population burden of stroke mortality continues to plummet in developed countries. For example, in the United States, among the 30 leading causes of death the 37% decline in age-adjusted stroke deaths between 1990 and 2010 was only exceeded by a 68% decline from HIV/AIDS, a 44% decline from ischemic heart disease, and a 39% decline from lower respiratory tract infections. However, data from the US Greater Cincinnati/Northern Kentucky Study suggest that between 1993/1994 and 2005 stroke rates are falling only for those aged ≥55 years, and there has been a 55% (83/100,000→128/100,000) increase for blacks aged 20 to 54 years, and a 92% (26/100,000→48/100,000) increase for whites of the same age. Although declines in stroke mortality and incidence in the United States are encouraging, disparities exist for Hispanics (perhaps because of a higher stroke risk in native born than first-generation Hispanics) and blacks.

Individual Stroke Risk and Trigger Factors

Traditional Risk Factors (Defined by the Framingham Stroke Risk Function)

Advances have been made to further understand the impact of the well-established risk factors. Not only the presence of diabetes mellitus, but also its duration may be an important factor. Compared with those free from diabetes mellitus, the risk of stroke was 1.7× greater for persons with diabetes mellitus of duration <5 years, 1.8× greater for duration of 5 to 10 years, and 3.2× greater for duration of ≥10 years. The finding that short-term diabetes mellitus may play a lesser role is supported by a meta-analysis showing pre-diabetes mellitus to have at most a modest impact on stroke risk.

A higher prevalence of hypertension is a contributor to the 3× higher risk of stroke among blacks aged 45 to 64 years, as is the lower blood pressure control. There also seems to be a racial difference in the effect of high blood pressure, where a 10-mmHg difference in systolic blood pressure is associated with an 8% increase risk in stroke in whites but a 24% increase risk in stroke among blacks.

The American Heart Association has suggested the Life’s Simple 7 (including blood pressure, cholesterol, glucose, body mass, smoking, physical activity, and diet) could serve as a clinically useful metric summarizing the traditional risk factors, and this scale is strongly associated with stroke, primarily through the blood pressure, glucose, and smoking components of the scale.

As assessment of predictors of intracerebral hemorrhage showed higher risk in men, those with higher levels of systolic blood pressure, and those using Warfarin. The intracerebral hemorrhage risk was high for young blacks but did not increase dramatically with age; in contrast, the risk in young whites was lower than in young blacks but risk increased dramatically with age so that older whites were at higher risk than older blacks.

Non-Framingham Risk Factors

Blood/Urine Biomarkers

Blood and serum biomarkers are a promising arena to identify powerful predictors of incident stroke. Although most often considered a biomarker for prevalent heart failure, N-terminal pro-B-type natriuretic peptide may be a powerful predictor for incident stroke, where in the Atherosclerosis Risk in Communities (ARIC) study the hazard ratio associated with the highest quintile of N-terminal pro-B-type natriuretic peptide was 2.70 (95% confidence interval [CI], 1.92–3.79) for total stroke and 6.26 (95% CI, 3.40–11.5) for cardioembolic stroke. Likewise, although albumin-to-creatinine ratio is thought to be an index of prevalent kidney disease, a ratio >300 mg/g is associated with a 2.70× (95% CI, 1.58–4.61) increase in stroke risk in blacks but only a 1.25× (95% CI, 0.62–2.51) risk in whites (relative to a albumin-to-creatinine ratio of <10 mg/g). Although adiposity was not associated with stroke risk, there was more than a doubling of risk (hazard ratio, 2.03; 95% CI, 1.27–3.27) between the top and bottom quartile of leptin levels in the British Regional Heart Study. Finally, serum fatty acid levels may be a powerful predictor of stroke risk, where, for example, there is a 1.38× (95% CI, 1.05–1.83) increase in stroke risk per SD change in linoleic acid.

Dietary Factors

A summary of recent publications assessing the association of dietary intake and stroke risk is beyond the scope of this review; however, a strong association between salt intake and stroke risk was demonstrated by the Northern Manhattan Study, with more than a 17% increase in stroke risk for each 500-mg/d increase in...
salt intake, an association that was not attenuated by adjustment for risk factors including hypertension.\textsuperscript{15} Also, noteworthy were 3 reports showing a significant decrease in the risk of stroke incidence associated with increases in coffee or tea consumption.\textsuperscript{6–10} Selected dietary flavonoids, specifically flavones and flavanones, that are contained, for example, in citrus fruits, were also shown to provide protection from stroke for women; however, replication of these observations is important as total flavonoids and other specific subclasses showed no association.\textsuperscript{19} Meta-analyses showed 19\% (10\%–27\%) decreased stroke risk with higher chocolate consumption,\textsuperscript{20} an 11\% (3\%–20\%) increase with higher levels of red meat,\textsuperscript{21} and a 12\% (3\%–20\%) decrease in the lowest quintile of low-fat dairy intake.\textsuperscript{22}

**Environmental/Geographic Factors**

The association of environmental exposures with stroke is less established than the relationship with heart disease. The relationship was not substantially clarified by a report that showed a relationship only between differences in particulate matter <10 μm (PM\textsubscript{10}) and ischemic stroke for those aged 65 to 79 years (and not NO\textsubscript{2}, or all ages for PM\textsubscript{10} or NO\textsubscript{2}, or all stroke),\textsuperscript{23} or a report by Andersen et al\textsuperscript{24} that showed marginally significant associations with exposure to NO\textsubscript{2}.

Although the specific factor contributors to higher stroke risk associated with living in the Stroke Belt remains mysterious, a marginally larger risk for stroke as an adult associated with residence during childhood (aged 0–12 years) and adolescence (aged 13–18 years) than other ages.\textsuperscript{25}

**Psychosocial Factors**

Appreciation of the role for psychosocial factors to influence stroke risk continues to grow and is supported by a study showing strong association between depression symptoms (Center for Epidemiologic Studies Depression Scale - 10 [CESD-10] score ≥10 or being on antidepressive medication) and stroke risk (odds ratio, 2.41; 95\% CI, 1.78–3.27).\textsuperscript{26} The possibility of an association between depression symptoms and stroke risk was also shown to be stronger among women.\textsuperscript{27} The association of environmental exposures with stroke is not fully understood and needs further investigation.

**Physical Activity and Obesity**

Huerta et al\textsuperscript{28} reported an inconsistent relationship between physical activity and stroke risk in the a large Spanish cohort, where increased recreational physical activity (but not physical activity at work or household physical activity) reduced risk in women, but associations were not shown in men for any type of physical activity. This was at some conflict with the findings of McDonnell et al\textsuperscript{29} who showed increased stroke risk among those with low levels of self-reported activity.

Stevens et al\textsuperscript{30} reported that substantial long-term weight gain was associated with increased ischemic stroke risk (hazard ratio, 1.38; 95\% CI, 1.04–1.84); however, the report failed to discuss changes in hypertension and diabetes mellitus that are potential in the pathway.

**Conclusions**

The pace of understanding the risk factors for stroke continues to increase, and further investments will continue to contribute to the declines in the burden of stroke.

**Disclosures**

None.

**References**

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Key Words: epidemiology ■ stroke
In developed countries, stroke mortality has decreased significantly. For example, in the United States, between 1990 and 2010, age-adjusted stroke mortality decreased by 37% to the fourth leading cause of death, after HIV/AIDS (down 68%), ischemic heart disease (down 44%), and lower respiratory infections (down 39%) [1]. The Greater Cincinnati/Northern Kentucky study compared data from 1993-1994 with 2005 and found that stroke incidence only decreased in people aged 55 and older, while stroke incidence was increased by 55% (from 83/100,000 to 128/100,000) in black people aged 20-54, and by 92% (from 26/100,000 to 48/100,000) in white people aged 20-54 [2].

While stroke mortality and incidence have decreased significantly in the United States, there are differences among Hispanic and black populations; possible explanations include higher stroke risk in Hispanic people born in the United States than in Hispanic people born in the United States [4] and stroke risk in black populations [5].

Individual Stroke Risk and Risk Factors

Traditional Risk Factors (Framingham Stroke Risk Factor)

Many studies have shown that diabetes mellitus is an important risk factor. Compared with people without diabetes mellitus, people with type 2 diabetes mellitus had a 1.7 times higher risk of stroke [6]. A meta-analysis of diabetes duration showed that diabetes duration >5 years increased the risk of stroke by 1.7 times, diabetes duration 5-10 years increased the risk of stroke by 1.8 times, and diabetes duration ≥10 years increased the risk of stroke by 3.2 times [7]. A meta-analysis of diabetes duration showed that diabetes duration >5 years increased the risk of stroke by 1.7 times, diabetes duration 5-10 years increased the risk of stroke by 1.8 times, and diabetes duration ≥10 years increased the risk of stroke by 3.2 times [7]. A meta-analysis of diabetes duration showed that diabetes duration >5 years increased the risk of stroke by 1.7 times, diabetes duration 5-10 years increased the risk of stroke by 1.8 times, and diabetes duration ≥10 years increased the risk of stroke by 3.2 times [7].

Blood/urine biomarkers

Blood and urine biomarkers have been shown to be promising stroke risk markers. Although N-terminal B-type natriuretic peptide is traditionally considered a biomarker for heart failure, it is also a strong predictor of stroke. In the Atherosclerosis Risk in Communities (ARIC) study, the highest quintile of N-terminal B-type natriuretic peptide had a HR of 2.70 (95% CI, 1.92-3.79) for stroke, and the highest quintile of N-terminal B-type natriuretic peptide had a HR of 6.26 (95% CI, 3.40-11.5) [11]. Similarly, a meta-analysis of white and black people showed that white people had a HR of 1.25 (95% CI, 0.62-2.51) for stroke, while black people had a HR of 2.70 (95% CI, 1.58-4.61) [12]. Although obesity and stroke risk are not strongly related, in the British Regional Heart Study [13], the highest quartile of weight loss was associated with a HR of 2.03 (95% CI, 0.62-2.51) for stroke.

Dietary factors

This article did not include recently published studies that assessed the relationship between dietary intake and stroke risk. However, the North Manhattan Study showed that high salt intake was strongly associated with stroke risk, with a 17% increase in stroke risk per 500 mg increase in sodium intake, and the association remained significant after adjusting for blood pressure [15]. Interestingly, three studies showed that increased coffee or tea intake was associated with a decrease in stroke risk [16-18]. Selective intake of flavonoids, especially flavonols and flavanones, found in citrus fruits, may also lower stroke risk in women [19]. A meta-analysis showed that those who consumed more chocolate had a 19% decrease (10%-27%) in stroke risk, and those who consumed more red meat had a 11% increase (3%-20%) in stroke risk [20], and those who consumed more low-fat food had a 12% decrease (3%-20%) in stroke risk [21].

Environmental/geographical factors

Environmental exposure to stroke is not as well studied as it is for other diseases. A study showed that particulate matter <10µm (PM10) was associated with ischemic stroke in the elderly [23]. Wilson et al. [24] also showed that particulate matter <10µm (PM10) was associated with ischemic stroke in the elderly [23].
显著相关。虽然在卒中高发带，使卒中风险增加的具体原因尚未阐明，但成年人的卒中风险与儿童期（0–12岁）和青春期（13–18岁）的居住地有很大的相关性，而非其他年龄段 [25]。

社会心理因素

社会心理因素对卒中风险的影响日渐受到关注。一项研究 (CESD-10) 显示抑郁症状和卒中风险有很强的相关性（OR，2.41, 95% CI, 1.78-3.27） [26]。Wilson 等人 [27] 的报告显示童年遭遇较高水平的情感忽视会导致成年后发生脑梗死的风险增加至2.8倍。

结论

对卒中危险因素的认识步伐不断增加，投入也将继续增加以降低卒中的负担。

参考文献

疫学研究の進歩
Population Studies 2013

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先進国の脳卒中死亡率は減少している。1990 ～ 2010 年、米国の脳卒中死亡率の減少は37%で HIV/AIDS、虚血性心疾患、下部気道疾患に次いで大幅であるが、ヒスパニックと黒人では必ずしも減少していない。最近注目される脳卒中の危険因子／誘発因子につき述べる。

古典的な危険因子（Framingham Stroke Risk Score に含まれる危険因子）
糖尿病では病歴5年未満で1.7倍、5 ～ 10年で1.8倍、10年以上で3.2倍と脳卒中リスクが増加する。中年の黒人は高血圧により脳卒中リスクが3倍増加する \(^1\)。血圧、コレステロール、血糖、肥満、喫煙、運動、食事からなる Life’s simple 7 スコアは従来の危険因子を集約する尺度で、特に血圧、血糖、喫煙の影響が大きい \(^2\)。脳出血は男性、高血圧、ワーカソの使用と関連し、老人黒人に多いが加齢で変化しない。一方、若齢者人のリスクは低いが加齢で増加するため、高齢者人は老人黒人よりリスクが高くなる。

Framingham Risk Score に含まれない危険因子
血液・尿のバイオマーカーでは、ARIC 研究でNT-proBナトリウム利尿ペプチドの最上位5分位は最低位に比べ全脳卒中が2.7倍、心原性脳塞栓症が6.26倍多かった \(^3\)。アルブミン / クレアチニン比が300 mg/gを超えると、脳卒中リスクは 10 mg/g 以下と比べ黒人が2.7倍、白人が1.25倍となった。レプチンの4分位下位と比較して、最上位では脳卒中リスクが高増し、リノン酸は1 SD の増加で1.38倍増加した。

食事因子については、Northern Manhattan Study において塩分摂取が1日500 mg の増加で脳卒中リスクが 17% 上昇した \(^4\)。コーヒー、お茶に関しては、3つの報告でいずれも脳卒中リスクが減少した。柑橘類に含まれるフラボノイド類は女性の脳卒中リスクを減少とする報告があるが、関連なしとする結果もある。メタ解析では、チョコレート摂取は最上位 4分位で19%の減少、赤身肉は11%の増加、低脂肪乳製品は最下位5分位で12%の減少を示した。

環境・地理的因子では、PM10 や二酸化窒素 (NO₂) と脳卒中リスクの関連が示唆された。米国のStroke Belt と脳卒中関連はいまだ謎であるが、小児期や青年期の居住により成人発症がわずかに増加する。精神的因子では、抑うつ、抗うつ剤使用と脳卒中の間の強い相関がある \(^5\)。小児期の感情的ネグレクトは成人の脳卒中リスクを2.8倍増加させる。運動と肥満については、スペインにおいて、レクリエーションが女性の脳卒中リスクを減らしたが、男性では効果がなかった。運動の体重増加は虚血性脳卒中を1.38倍増加させたが、高血圧や糖尿病の関与は否定できない。

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引用文献