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.1 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% (83/100000→128/100000) increase for blacks aged 20 to 54 years, and a 92% (26/100000→48/100000) increase for whites of the same age.2 Although declines in stroke mortality and incidence in the United States are encouraging, disparities exist for Hispanics3 (perhaps because of a higher stroke risk in native born than first-generation Hispanics)4 and blacks.5

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.6 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.7

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.8

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.9,10

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.8

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.11 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).12 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.13 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.14

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

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salt intake, an association that was not attenuated by adjustment for risk factors including hypertension. Also, noteworthy were 3 reports showing a significant decrease in the risk of stroke incidence associated with increases in coffee or tea consumption. 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. Meta-analyses showed 19% (10%–27%) decreased stroke risk with higher chocolate consumption, an 11% (3%–20%) increase with higher levels of red meat, and a 12% (3%–20%) decrease in the lowest quintile of low-fat dairy intake.

**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 (PM₁₀) and ischemic stroke for those aged 65 and not NO₂, or all ages for PM₁₀ or NO₂, or all stroke, or a report by Andersen et al. to discuss changes in hypertension and diabetes mellitus that may or may not influence stroke risk continues to grow and is supported by a study showing the findings of McDonnell et al. that showed marginally significant associations with exposure to NO₂.

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. The impact of pre-diabetes on future risk of stroke: meta-analysis. BMJ. 2012;344:e3564.

**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). The possibility of childhood exposures playing a major role on the risk of adult stroke was supported by a report of Wilson et al. describing a risk of infarction 2.8× greater for those reporting a moderately high level of childhood emotional neglect.

**Physical Activity and Obesity**

Huerta et al. 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. who showed increased stroke risk among those with low levels of self-reported activity. Stevens et al. 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**


Key Words: epidemiology ■ stroke

**个体卒中风险和诱因**

**传统的危险因素（Framingham卒中危险因素）**

很多研究进展能更进一步理解这些危险因素的影响。除糖尿病本身，病程时间也是一个重要因素。相比非糖尿病患者，糖尿病病程<5年患者的卒中风险为1.7倍，病程5-10年的患者为1.8倍，病程≥10年的患者为3.2倍[6]。一项meta分析表明糖尿病前期对卒中风险至多有轻微影响[7]，这证实了短期糖尿病对卒中风险影响很小。

在45-64岁的黑人，由于较高的高血压发病率和较低的血压控制率，导致这部分人群的卒中风险升至3倍。高血压对卒中的影响似乎也存在种族差异，收缩压每升高10mmHg，白人的卒中风险增加8%，而黑人却增加24%[8]。

美国心脏协会（AHA）建议的Life’s Simple 7（包括血压，胆固醇，血糖，体重，吸烟，体力活动和饮食）可作为衡量传统危险因素的一个非常有用的临床标准。这个测定标准与卒中风险紧密相关，尤其血压，血糖和吸烟[9,10]。

脑出血风险评估研究显示：男性、高收缩压、使用华法林都是脑出血的危险因素。青年黑人发生脑出血的风险较高，但随着年龄这一风险并未显著增加。相反，青年白人发生脑出血的风险较低，但却随着年龄风险急剧增加，因此，老年白人的脑出血风险要高于老年黑人[8]。

**非Framingham卒中危险因素**

**血/尿生物标记物**

血液和血清生物标记物被认为是一种很有前景的卒中风险预测方法。虽然N端-B型利钠肽前体通常被认为是心衰的生物标志物，但其可能也是卒中的强有力预测因子。社区动脉粥样硬化研究（ARIC）中，将N端-B型利钠肽前体水平进行五分位，最高分位组的卒中风险比（HR）为2.70（95% CI, 1.92-3.79），心源性卒中的风险比为6.26（95% CI, 3.40-11.1）[11]。同样，虽然白蛋白/肌酐比被认为是对普通肾脏疾病的诊断指标，在黑人当比值>300mg/g时，相比<10mg/g，卒中风险增加2.3倍（95%CI, 1.58-4.61），而白人卒中风险仅增至1.2倍（95%CI, 0.62-2.51）[12]。虽然肥胖与卒中风险并不相关，但在英国地区性心脏研究[13]中发现，瘦素水平最高分位组的卒中风险是最低分位组的两倍多（HR 2.03, 95% CI 1.27-3.27）。最后，血清脂肪酸水平也可能是卒中风险的一个强有力预测因素，如亚麻酸水平每升高一个标准差卒中风险增加1.38倍（95% CI, 1.05-1.83）[14]。

**饮食因素**

本文未纳入最近发表的评估膳食摄入与卒中风险相关性的文献。然而，北曼哈顿研究证明盐摄入量与卒中风险强烈相关，盐摄入量每增长500mg/d，卒中风险增加17%多，校正包括血压的其他危险因素后，此相关性无变化[15]。值得注意的是，有3份报告表明增加咖啡或茶摄入与卒中风险显著下降相关[16-18]。选择性摄入黄酮类化合物，特别是黄酮和黄烷酮类，例如柑橘类水果含有，也可降低女性卒中风险。然而，重复这些观察性研究很重要，因为总黄酮和其他特定亚类与降低卒中风险无相关性[19]。一项荟萃分析结果显示，巧克力摄入较高的人群卒中风险降低19%（10% -27%）[20]，红肉摄入较高的人群卒中风险增加11%（3% -20%）[21]，低脂饮食五分位最低分位的人群卒中风险下降12%（3% -20%）[22]。

**环境/地理因素**

环境暴露与卒中的相关性还未像心脏疾病那样研究得透彻。只有一篇报道显示了颗粒物<10μm(PM10)与65-79岁人群的缺血性卒中相关，但未详细阐明[23]。Wilson等人[24]也报道二氧化氮暴露与卒中
虽然在卒中高发带，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]的报告指出，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。

体育活动和肥胖

在西班牙一项大规模队列研究中，Huerta 等人[28]报道，体力活动和卒中风险的关系并不一致，娱乐性运动增加(而不是工作中或家庭的体力活动和肥胖)可降低女性卒中风险，但男性卒中风险与任何类型的体力活动无相关性。这与McDonnell等人[29]报道的结果有些冲突，该结果显示在自我报告较少体力活动的人群中，卒中风险增加。

Stevens等人[30]报道，长期体重过重可增加缺血性卒中的风险（HR1.38, 95% CI, 1.04–1.84），但是该报告却未讨论高血压和糖尿病的变化在此作用路径中的潜在作用。

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

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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、脳卒中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倍と脳卒中にリスクが増加する。中年の
黒人では高血圧により脳卒中にリスクが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、ターザリンの使用と関連し、若齢黒人で多いが加齢で加味しない。一方、若齢白人のリスクは低いが加齢で増加するため、高齢白人は老齢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ナトリウム利尿薬ペプチドの最上位5%位は最
下位で全脳卒中が2.7倍、心原性脳死検査が6.2倍
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 以下と比べ黒人で
2.7倍、白人で1.25倍となった。レプチンの4分位
下位位と比較して、最上位では脳卒中リスクが増加し、
リノレン酸が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らすとの
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も位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 と脳卒中リスク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、抗うつ薬使用と脳卒中の関に強
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。長期の体
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。

引用文献