An unfavorable dietary pattern is associated with symptomatic ischemic stroke and carotid atherosclerosis

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Objective: Ischemic strokes represent more than 80% of total strokes in Western countries. The influence of dietary factors on ischemic stroke risk is debated mainly because available data are limited. Our objective was to compare the dietary pattern of symptomatic ischemic stroke patients under 65 years old with control subjects using a validated 14-item food frequency questionnaire (FFQ). We also compared symptomatic ischemic stroke patients with carotid atherosclerosis with those without according to the presence or the absence of carotid plaque defined by duplex scanning.

Methods: This was a case-control multi-center study that took place in one University hospital and two general hospitals in France. One hundred twenty-four symptomatic ischemic stroke patients (confirmation by a neurologist and imaging: 66% smokers) and 50 controls (34% smokers) without any known cardiovascular disease or previous nutritional advice were included. The main outcome measure(s) were intake scores for saturated (SFA), monounsaturated (MUFA), Ω-3 polyunsaturated (Ω-3 PUFA), and Ω-6 polyunsaturated fatty acids (Ω-6PUFA). Fruit and vegetables and an overall cardiovascular dietary score were evaluated with the FFQ. The overall cardiovascular score is calculated as (MUFA + Ω-3PUFA + fruits and vegetables) - (SFA) scores.

Results: Compared with controls, ischemic stroke patients had a higher SFA score (6.6 ± 3.0 vs 4.9 ± 2.7; P < .001), lower scores of MUFA (0.8 ± 0.9 vs 1.5 ± 1.2; P < .001), Ω-3 PUFA (1.7 ± 1.6 vs 2.2 ± 1.8; P = .013), Ω-6PUFA (2.6 ± 2.5 vs 3.9 ± 2.7; P = .002), fruit and vegetables (2.9 ± 1.7 vs 3.8 ± 1.6; P = .005), and a lower overall dietary score (−1.2 ± 5.0 vs 2.5 ± 4.4; P < .001). These results remained statistically significant after adjustment for age, gender, and smoking status. Ischemic stroke patients with carotid atherosclerosis (n = 54) had a worse overall cardiovascular dietary score than those without (n = 68): −2.2 ± 4.4 vs −0.2 ± 5.2; P = .024.

Conclusion: Compared with controls, ischemic stroke patients, especially those with carotid atherosclerosis, have an unfavorable dietary pattern (high SFA, low fruit and vegetables, and Ω-3 PUFA consumptions) that may have been a facilitating condition of the ischemic stroke. Dietary recommendations of a healthy diet should be useful in ischemic stroke prevention, especially in patients with cardiovascular risk factors. (J Vasc Surg 2010;52:62-8.)

Strokes account for one of every 17 deaths in the United States and are the leading cause of long-term disability.1 The estimated direct and indirect cost of strokes is €34 billion Euros in the European Union for 2003.2 Ischemic strokes account for 87% of all strokes.3 Diet plays a major role in ischemic coronary heart disease (CHD), and dietary patterns such as a Mediterranean diet can lower CHD mortality.3,4 CHD and ischemic strokes share several major risk factors, and the ischemic stroke rate is indeed reduced by a healthy lifestyle.5 However, the influence of diet, in particular fat intake, on ischemic stroke risk is debated,6-8 and data are limited. Ischemic strokes can be the consequence of different etiological processes, which could be associated or not with dietary patterns. Furthermore, most of the available tools (diet interviews, diet records, large food frequency questionnaire [FFQ]) used to evaluate an individual diet are too complicated and time-consuming for routine clinical practice and population screening. The primary objective of our study was to compare the dietary pattern of symptomatic ischemic stroke patients (SISP) with control subjects using a validated 14-item FFQ.9,10 Our secondary objective was to compare SISP with carotid atherosclerosis with SISP without carotid atherosclerosis according to the presence or the absence of carotid plaque defined by duplex scanning. We hypothesized that the presence of a carotid atherosclerosis might be associated with a more unfavorable diet, as it has already been reported in patients with coronary atherosclerosis.11
MATERIALS AND METHODS

This case-control multicenter study was conducted in France in accordance with French medical laws. All participants were Caucasian residents and gave their informed consent.

Populations

Ischemic stroke patients. All SISP were consecutively recruited, over a 5-month period, in two general hospitals (St Brieuc, Vannes) and one university hospital (Rennes). Inclusion criteria were age $\leq$ 65 years old, and symptomatic ischemic stroke confirmed by a neurologist and computerized tomography (CT) scanning or magnetic resonance imaging (MRI). Only participants aged below 65 years old were included to minimize the influence of dietary changes due to aging or the occurrence of other health problems. Exclusion criteria were presence of CHD or history of CHD, and death within the 48 hours after the admission. Patients with an associated CHD were excluded because CHD is known to be frequently associated with an adverse dietary pattern, which could have induced a possible bias in the dietary assessment. All ischemic strokes were confirmed by CT scanning and/or MRI that allowed the exclusion of other neurological causes. Patients were classified by a neurologist according to the etiological Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification and to the Rankin Disability Scale before discharge. The TOAST classification is a validated index of stroke origins: TOAST 1: large-artery atherosclerosis origin; TOAST 2: cardio-embolism origin; TOAST 3: lacunar origin; TOAST 4: other determined origin (eg, dissection); and TOAST 5: undetermined origin, because two or more origins were identified or the stroke was cryptogenic. The Rankin Scale is a validated handicap index after stroke. The prevalence of hypertension, dyslipidemia, and diabetes was noted if patients were receiving a medication for these conditions prior to the episode of stroke. Carotid atherosclerosis was assessed in stroke patients by duplex scanning. Carotid plaque was defined as a focal structure that encroaches into the arterial lumen of at least 0.5 mm or 50% of the surrounding intima-media thickness value or demonstrates a thickness $>1.5$ mm as measured from the media-adventitia interface to the intima-lumen interface, according to the definition of the Mannheim conference consensus.

Control subjects. Control subjects were consecutively recruited in a health appraisal center. Inclusion criteria were age $\leq$ 65 years old, no history of cardiovascular or metabolic diseases, normal neurological and cardiovascular examination (including peripheral artery examination and electrocardiogram), and no previous nutritional advice. All control subjects lived in the same region (Brittany, France) as the patients.

Dietary assessment

We used a short FFQ, previously validated for food assessment in CHD prevention, that allows assessment of the dietary pattern prior to the questionnaire administration. This semi-quantitative FFQ is constructed with 14 questions selected to give information about the intake of food groups likely to influence CHD risk. A group of six questions explored the saturated fatty acids (SFA) intake from cheese, red meat, delicatessens, salted pies and pizzas, cookies, cakes and pastries, and butter. Another group of five questions explored vegetable mono-un-saturated fatty acids (MUFA) and $\Omega$-3 and $\Omega$-6 poly-saturated fatty acids (PUFA) intake from fish, nuts, and vegetable fats. A last group of four questions explored the intake of fruits and vegetables (for more details, see9). A specific score is calculated for SFA, MUFA, $\Omega$-6 PUFA, $\Omega$-3 PUFA, and fruit and vegetables. An overall cardiovascular dietary score is calculated as $(\text{MUFA} + \Omega - 3 \text{ PUFA} + \Omega - 3 \text{ PUFA}) - (\text{SFA})$ scores. It finally allows an estimation of the dietary pattern graded from −17 to +19. The higher the score, the more favorable the dietary pattern. The administration of this FFQ needed 5 to 10 minutes and was administered within the first 3 days following the onset of stroke. Thanks to relative proximity of the three centers, the evaluation was performed by the same investigator to avoid inter-observer variability. In case of aphasia, the spouse answered the FFQ. Plasma content of vitamin C, which is a biomarker of fruit and vegetable intake, was measured in the 55 patients included at the University hospital.

Statistical analysis

Statistical analysis was performed with SAS statistical software V9.1 (SAS Institute, Cary, NC). The mean $\pm$ SD are reported for continuous variables, and the number of patients in each category for categorical variables and the corresponding percentage are given. The two groups were compared using the Student’s $t$ test or Wilcoxon rank-sum test when appropriate for continuous variables, and the chi square or Fisher’s exact test when appropriate for categorical variables. Firstly, control subjects were compared with SISP. This analysis was adjusted for age, gender, and smoking status, since these characteristics were not well balanced between the two groups. Then, a subgroup analysis also compared dietary scores of SISP with and without carotid atherosclerosis. Spearman correlation coefficients were calculated between plasma content of vitamin C and questions about fruit and vegetables. For all analyses, a value of $P < .05$ was considered as statistically significant.

RESULTS

A total of 138 consecutive SISP were screened in the three participating centers. Seven patients died during the acute phase, and seven others were excluded due to an associated CHD. Finally, 124 SISP were included, including 37 transient ischemic attacks as defined by the ad hoc committee of strokes and 87 ischemic strokes. A history of medication for hypertension, diabetes, or dyslipidemia was present in 20%, 7%, and 22% of stroke patients, respectively. The medical management of stroke patients was performed according to the recent guidelines. ToAST classification 1, 2, 3, 4, and 5 represented 10% (n = 13), 7% (n = 9), 5% (n = 6), 12% (n = 15), and 65% (n = 81),
The plasma vitamin C determined in 55 SISP was well presented 43% (n = 53), 19% (n = 23), 16% (n = 20), 4% (n = 5), 17% (n = 21), and 1% (n = 1), respectively (data is missing for one of the scores). Thirty-three percent of the women with a stroke were taking an estrogen therapy. Alcohol consumption was <10 g/day in 67 patients, 10 g/day in 25, 20 to 30 g/day in 27, and ≥40 g/day in 5.

The population of controls was composed of 50 subjects. The characteristics of these two subgroups were similar, but the patients without atherosclerosis were slightly younger (49 vs 56 years old; P = .001), with a higher proportion of women (44% vs 22%; P = .011) and a higher proportion of estrogen users among women (37% vs 17%). There was no significant difference in alcohol consumption between patients without and with atherosclerosis; 46% and 48%, respectively, were drinking ≥10 g alcohol daily. Stroke patients with carotid atherosclerosis had a significantly lower overall cardiovascular dietary score (P = .024) resulting from trends toward a higher intake of SFA and lower intakes of MUFA, ω-3 PUFA, and fruit and vegetables (Table IV). The TOAST 1 subgroup had the highest scores for SFA (7.3 ± 3.2), the lowest scores for MUFA (0.4 ± 0.7), ω-3 PUFA (1.2 ± 1.6), fruits and vegetables (1.7 ± 1.4), and the lowest overall cardiovascular dietary score (−4.0 ± 5.1; Table V).

**DISCUSSION**

This study showed, in a French Caucasian population, that SISP had an unfavorable diet prior to stroke. This unfavorable diet was characterized by higher intake of SFA but a lower intake of MUFA, ω-6 and ω-3 PUFA, and fruit and vegetables. Another interesting contribution of the present study was that the results we showed were obtained using a FFQ only based on 14 questions.

The relationships between diet and stroke are controversial and relatively sparse. The different etiologies of ischemic strokes may be linked differently to risk factors and, in particular, dietary factors. Our study investigates these associations in a French population. France is characterized by a large diversity in dietary habits that facilitates this evaluation. The FFQ we used is a simple 14-item tool, but it has a good reproducibility and has been validated against a reference method and biomarkers. It gives intake scores for different food groups and an overall cardiovascular score associated with coronary risk.

The associations between dietary fats, in particular SFA, and stroke risk are the most debated. Although SFA intake represents a major component of the Western dietary pattern and is strongly associated with CHD risk, studies have reported no association, a positive association, and even an inverse association with ischemic stroke risk. In our FFQ, we only consider the vegetable source of MUFA, mainly from olive or canola oils and margarines. MUFA intake of stroke patients was almost half that of controls. In the Omni-Heart trial, a diet rich in MUFA was associated with a better blood pressure lowering effect, which could result in a reduction of stroke risk. A high level of vegetable MUFA intake is also a marker of a Mediterranean-type diet and has been associated with a lower risk of stroke.

The FFQ used assesses the ω-3 PUFA intake both from marine and vegetable sources. Fish consumption is the

**Table I.** General characteristics of the subjects in each studied group

<table>
<thead>
<tr>
<th>Symptomatic ischemic stroke patients (n = 124)</th>
<th>Controls (n = 50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>47 ± 10</td>
<td>52 ± 10</td>
</tr>
<tr>
<td>Men, number</td>
<td>22 (44%)</td>
<td>81 (65%)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.3 ± 3.2</td>
<td>26.0 ± 5.1</td>
</tr>
<tr>
<td>High school level</td>
<td>42 (84%)</td>
<td>84 (67%)</td>
</tr>
<tr>
<td>Current or former smoker</td>
<td>17 (34%)</td>
<td>81 (66%)</td>
</tr>
<tr>
<td>Sedentary</td>
<td>17 (34%)</td>
<td>61 (50%)</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>5.47 ± 0.95</td>
<td>5.28 ± 1.14</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>0.87 ± 0.32</td>
<td>1.54 ± 0.99</td>
</tr>
</tbody>
</table>

BMI, Body mass index; sedentary, less than 20 minutes walking per day. Values are mean ± SD for quantitative variables and n (%) for qualitative variables.
source of long-chain Ω-3 PUFA and has been inversely correlated with ischemic stroke risk. The potential antiarrhythmic effect of long-chain Ω-3 PUFA could also be involved in the risk reduction of strokes related to atrial tachyarrhythmias. The serum content of alpha-linolenic acid, provided from oils and margarines in this FFQ, has also been found to be inversely correlated with stroke risk.

A lower consumption of Ω-6 PUFA was found in SISP, as it was reported in a Japanese population, but the proportion of lacunar infarction in that study was high.

The fruit and vegetable consumption has been consistently associated with a lower stroke risk. The Dietary Approaches to Stop Hypertension (DASH) diet is rich in fruits and vegetables, lowers blood pressure (BP), and also reduces the incidence of stroke.

Fruits and vegetables are rich in potassium. Potassium intake itself is associated with a lower risk of stroke that can be linked to its BP lowering effect. The high content of antioxidants is another characteristic of a diet rich in fruits and vegetables. Dietary flavonoids can also lower the risk of stroke. Fruits are a major source of vitamin C, a high intake of which has been associated with a 42% lower risk of stroke.

Complex interactions between the different components of a diet may exist, and its effect cannot be attributed to an individual component of the diet but rather to a combination of dietary factors. A global index represented by the overall dietary score is therefore more suitable to assess the impact of diet. Very few studies have assessed the impact of an overall dietary pattern on stroke risk.
In American women, the risk of an ischemic stroke was increased by 56% with a Western pattern while a “prudent” diet was associated with a 26% decrease. Also, a DASH-style diet may reduce the incidence of stroke in women.

Another original contribution of this study concerns the differential impact of diet according to the presence or absence of atherosclerosis investigated by duplex scanning with a strict definition of plaques. This evaluation has shown a significant worse diet (overall dietary score) in patients with atherosclerosis compared with those without. There was also a trend to worse values for each score in the former group. Although the limited number of patients precludes any conclusion, the very unfavorable results noted in the TOAST 1 group (carotid atherosclerosis >50%) seem to confirm a closer relationship of a Western dietary pattern with strokes associated with carotid atherosclerosis. Carotid and coronary atherosclerosis share a common pathophysiology. Although some differences have been reported in the associations of carotid and coronary atherosclerosis with the major vascular risk factors, these risk factors facilitate the atherosclerosis process in both locations. Thus, it is not surprising to find a closer association between ischemic strokes with carotid atherosclerosis and dietary factors known to influence atherosclerosis in other locations.

This study presents some limitations. First, all patients were relatively young (52 ± 10 years old), because we wanted to minimize the influence of dietary changes due to aging or the occurrence of other health problems. Second, since we did not perform imaging in control subjects, we cannot exclude that some of the controls could have experienced a silent asymptomatic ischemic stroke. However, they had no such history, and their examination was normal. Third, we cannot exclude that some SISP with hypertension, diabetes, or dyslipidemia could have modified their diet because of their disease and/or risk factors. However, these dietary modifications would have probably improved their dietary scores and decreased the dietary score differences between SISP and control subjects. Finally, SISP are not strictly matched to controls and, without surprise, they tended to have a more unfavorable lifestyle. Moreover, since we did not perform imaging in control subjects, the overall cardiovascular score appeared statistically different when we compared stroke patients with atherosclerosis with patients without, whereas their risk factors were not different (smoking status, dyslipidemia, diabetes, educational status, BMI, hypertension, family history).

**CONCLUSION**

This study showed that compared with controls, ischemic stroke patients, especially those with carotid atherosclerosis, have an unfavorable dietary pattern characterized by a higher SFA intake, and lesser MUFA, Ω-3 PUFA, Ω-6 PUFA, and fruit and vegetable intakes. Dietary recommendations of a healthy diet should be useful in ischemic stroke prevention, especially in patients with cardiovascular risk factors.
factors. Interventional studies should be led to confirm these findings and to determine whether the dietary recommendations for CHD prevention could also apply to ischemic stroke prevention.

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Conception and design: GM, FP, TR
Analysis and interpretation: GM, BL, FP
Data collection: GM, TR, VG, TC
Writing the article: GM, BL, JB, FP
Critical revision of the article: GM, BL, FP
Final approval of the article: GM, TR, BL, FP
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REFERENCES

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