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Association of Dietary Factors with Progression of AA in Stroke/TIA Patients

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Abstract

Objective: To investigate the effect of dietary factors such as calorie intake and dietary fats on the progression of aortic arch atheroma (AA).

Background: In stroke/TIA patients, progression of AA is associated with recurrent vascular events.

Design/Methods: Consecutive patients with measurable (>1 mm) AA atheroma on baseline transesophageal echocardiogram (TEE) evaluation consented to a protocol mandated follow-up TEE at 12 months. Patients that had adequate paired AA images were assessed for progression, defined as Δ ≥ 1 grade worsening (based on plaque thickness over 12 months). Stroke risk factors and fasting lipid profile were assessed at baseline. The patient's nutritional intake was measured at baseline using the Gladys Block Food Frequency Questionnaire.

Results: One-hundred-nine patients (70 strokes, 33 TIAs) had sequential TEEs, of whom 27% (N=30) progressed and 73% (N=79) did not. Patients with progression had higher daily calorie (1778 ± 623 vs. 1378 ± 406 Calories, p=0.008), fat (76 ± 33 vs. 52 ± 23 grams, p=0.0002), carbohydrate (208 ± 78 vs. 169 ± 57 grams, p=0.01) and protein (73 ± 26 vs. 57 ± 21 grams, p=0.005) intake. On Further analysis among different fats showed a higher consumption of saturated fats (25 ± 12 vs. 17 ±8 grams, p=0.00051) as well as unsaturated fats (44 ± 20 vs. 30 ± 13 grams, p=0.002). These differences remained significant after we adjusted for the medication use. However the significance of these differences was attenuated after adjusting for the calorie intake. Cholesterol consumption did not differ between the progression and no-progression group (262 ± 125 vs. 213 ± 149 mg, p=0.2).

Conclusions/Relevance: Calorie intake plays a significant role in the progression of AA. Further studies are needed to confirm these findings and determine the specific dietary modifications that may prevent AA progression and associated recurrent vascular events.

Keywords: Diet; Caloric intake; Atheroma; Aortic arch; Cardiovascular

Introduction

Aortic arch atheroma (AA) has been known for its association with stroke [1-4] and is believed to be the potential source of embolic phenomenon leading to subsequent strokes [5-9]. It is reported that the progression of AA is associated with recurrent vascular events [10]. However, limited literature is available on the factors contributing to progression of AA in the stroke patient population [11,12]. AA is a dynamic process with significant rates of progression and regression over time [13,14]. AA ≥ 4 mm as an independent risk factor for incident and recurrent strokes [1,2].

Significant plaque, size ≥ 4 mm, in the aortic arch is the second most common source for recurrent cardio embolic phenomenon resulting in subsequent strokes [15,16]. Additionally progression of AA, may predict recurrent vascular events in stroke/TIA patients [13]. Therefore, prevention of atheroma progression may be important in the prevention of recurrent vascular event in the stroke/TIA population. Age, gender, heredity, hypertension, diabetes mellitus, hyperlipidemia, sedentary lifestyle and smoking have been suggested to be risk factors for aortic atheroma [17]. Studies have reported an association between hyperhomocysteinemia, [18,19] elevated cholesterol, [11] elevated WBC count [19], and fibrinogen level [20,21] with AA. Recently we reviewed the effect of medications –statins, antiplatelet agents and oral anticoagulants on aortic atheroma progression [22]. It is well known fact that there are several dietary risk factors influencing atherosclerosis and vascular events [23].

Although, the direct relationship between different dietary fats and atherosclerosis is evident [24-26] but its effect on AA progression is unknown. Few studies reported calorie restriction to be preventive for atherosclerosis [27-29] No previous clinical studies have reported the effect of dietary factors such as calorie intake or dietary fats on the progression of AA. In this study we report the effect of dietary factors including calorie intake on the progression of the AA among stroke and transient ischemic attack (TIA) patients.

Methods

Study population

367 patients with stroke and TIA were screened in the study. All patients received a Trans Esophageal Echocardiogram (TEE) as a part of their routine stroke workup to determine the stroke etiology. Acute stroke was confirmed using CT and/or MRI. Exclusion criteria included age <18 years, no measurable AA on first TEE (Plaque <1 mm in ascending or descending aorta), intracerebral hemorrhage, subarachnoid hemorrhage, coma and any other life threatening conditions. Of the 367 patients, 167 were eligible for the study and among them 125 consented for the present study. Only 109 of the 125 patients were considered to have measurable AA imaging on TEE, completed a 12-month TEE to assess for AA progression and thus only these patients were included in the analysis. The stroke risk factors and medications were recorded at baseline.

TEE assessment of AA

A detailed examination of AA was performed using a Hewlett-Packard 21364A Omni plane probe. Images of the proximal and mid ascending aorta on long axis were obtained at a depth of 30 cm and at an angle of 100-1500. The descending thoracic aorta was examined by advancing the probe distally into the esophagus and at an angle of 0°. The probe was withdrawn slowly to view more proximal segments and when the probe reached the aortic arch, the multiplane angle was rotated between 0° and 90° to acquire sequential short axis views. Images were captured from the diseased segments of aortic arch with an annotation of the distance from the probe to the incisors. The depth of the probe from incisors was used as the guide to image similar regions in the aortic arch a year later.

Two observers, blinded to the clinical data, quantified the measurements of the aortic atheroma independently for each imaged segment. Plaque thickness was measure as the maximal thickness of the intimal and medial layers and graded as mild (<1 mm), moderate (1-3.9 mm) and severe (>4 mm) [1]. Any increase in the maximal thickness of plaque in the aortic arch by greater than 1 grade was defined as progression. Satisfactory inter-observer reliability was noted among the two observers in the assessment of aortic plaque thickness in different segments of the aortic arch [17].

Dietary assessment

We used the Food Frequency Questionnaire (FFQ) [30] for dietary assessment of the stroke patients at baseline. The 1998 version of the diet block FFQ (Block 98) was used in order to convert information on the supplement consumption to average daily energy and nutrient intake using values from US Department of Agriculture nutrient database for standard. The block questionnaire is a quantitative tool that includes 109 food and beverage items and three multiple as well as nine single vitamin and mineral supplement items.

Data analysis

Daily calorie intake, total fat, protein, carbohydrate, cholesterol, and BMI were measured and tested for association with AA progression. We performed a one sample t-test with continuous variables and progression of AA. Furthermore, we adjusted for the medication used to treat the risk factors using the analysis of covariance (ANCOVA) procedure. The data analysis was carried out on SAS version 9.2 (Cary, NC).

Results

Mean age of the study population was 65 ± 12 years constituting 60% males and 81% Caucasians. Among the study population, 82% were with known hypertension and were on anti-hypertensives. 24% diabetic and were treated for same. 71% with hypercholesterolemia and only 47% were on statins. The mean BMI of the study population was 28 ± 6 and mean total calorie intake was 1496 ± 510 kcal/day. The average consumption of dietary fat was 59 ± 29 grams/day of which average unsaturated fat was 34 ± 17 grams/day and average saturated fat was 20 ± 10 grams/day. On average the protein intake was 61 ± 23 grams/day and total carbohydrate intake was 179 ± 64 grams/day. On further analysis among fats, we found an average consumption of oleic acid at 23 ± 12 grams/day and linolenic acid at 12 ± 6 grams/day. (Tables 1A and 1B) depicts the baseline risk factors and dietary characteristics among the stroke and TIA patients.

Risk factors and medications	Stroke/TIA patients (N=109)
Mean age (years)	65 ± 12
Male	65 (60%)
Caucasian	88 (81%)
Hypertension	89 (82%)
Diabetes	26 (24%)
Hypercholesterolemia	76 (71%)
Total cholesterol (mg/dl)	185 ± 40
LDL (mg/dl)	106 ± 37
HDL (mg/dl)	52 ± 17
Triglycerides (mg/dl)	153 ± 98
Smokers	23 (21%)
Alcohol use	26 (24%)
BMI	28 ± 6
Medication categories:	
Anti-hypertensive	89 (82%)
Diabetic medication	26 (24%)
Antiplatelet therapy	69 (63%)
Anti-coagulant therapy	21 (19%)
Statin drugs	51 (47%)

Table 1A: Baseline risk factors among stroke and TIA patients.

At baseline on the TEE measurement, the mean plaque thickness in the ascending aorta was 1 mm, in the arch of aorta was 3.5 mm and in the descending aorta was 4.2 mm. At the one year follow up visit on the TEE measurement, the mean plaque thickness in the ascending aorta was 1 mm, in the arch of aorta was 3.7 mm and in the

descending aorta was 4.2 mm. Amongst the 109 subjects, 27.5% (N=30) had progression of the AA. Stroke risk factors were more prevalent in the progression group compared to the rest of the population. Table 2 summarizes the risk factors in two subpopulations stratified by AA progression.

Nutritional factors	Stroke/TIA patients (N=109)	Contribution to total calories
Total calorie intake (Cal/day)	1496 ± 510	_
Total protein (grams/day)	61 ± 23	244 ± 92 cal
Total carbohydrate intake (grams/day)	179 ± 64	716 ± 256 cal
Total fat intake (grams/day)	60 ± 29	540 ± 261
Total cholesterol (mg/day)	221 ± 141	_

Table 1B: Baseline dietary characteristics among stroke and TIA patients.

The unadjusted mean calorie intake in those with progression of AA was (1778 ± 623) Kcal was higher compared to those without progression (1378 ± 406 Kcal, p=0.0008). Similarly, the consumption for daily fat were (76 ± 33 vs. 52 ± 23 grams, p=0.0002). Further analysis among different fats showed that both saturated fats (25 ± 12 vs. 17 ± 8, p=0.0005) and unsaturated fats (44 ± 20 vs. 44 ± 20, p=0.002) was higher in the progression group compared to the no progression group. Among the unsaturated fatty acids, linolenic (16 ± 8 vs. 10 ± 6 grams, p=0.001) and oleic acid (27 ± 13 vs. 20 ± 9 grams, p=0.0034) were distributed unevenly in the two groups. Upon further evaluation of the distribution of the carbohydrates, the mean consumption among the subjects with progression of the aortic arch plaque and among those with no progression was 208 ± 78 and 169 ± 57 grams/day respectively. The distribution of carbohydrates among the two groups did vary significantly (p=0.014). Similarly, there was difference in distribution of protein (73 ± 26 vs. 57 ± 21 grams, p=0.0054). The distribution of cholesterol (262 ± 125 vs. 213 ± 149 mg, p=0.168) did not vary among those who had progression of AA and those who did not. Table 3 summarizes the distribution of unadjusted dietary factors among the different groups of stroke and TIA patients.

	Progression (N=30)	No progression (N=79)
Mean age (years)	66 ± 11	65 ± 13
Male	18 (60%)	47 (59%)
Caucasian	24 (80%)	64 (81%)
Hypertension	27 (90%)	62 (78%)
Diabetes	12 (40%)	14 (13%)
Hypercholesterolemia	24 (80%)	53 (67%)
Smokers	7 (23%)	16 (20%)
Alcohol use	5 (17%)	21 (27%)
Average BMI	28 ± 7	28 ± 5
On anti-hypertensives	27 (90%)	62 (78%)
On diabetic medications	12 (40%)	14 (13%)
On antiplatelet therapy	18 (60%)	51 (64%)
On anti-coagulant therapy	5 (17%)	16 (20%)
On statins	11 (37%)	40 (50%)

Table 2: Risk factors in groups stratified by AA progression.

On adjusting for the medications used to treat the stroke risk factors among the different groups, the distribution of the dietary risk factors varied significantly among those with progression and no progression of AA. Table 3 summarizes the distribution dietary risk factors among the different groups of stroke and TIA patients after adjusting for the medication use. Table 3 also summarizes the distribution of dietary risk factors among the different groups of stroke and TIA patients after adjusting for total calorie intake. On further adjusting for total calorie consumption among the different groups, dietary factors did not significantly differ among those with progression when compared to no progression group.

Dietary factors	Progression (N=30)[1]	No progression (N=79)[1]	Progression (N=30)[2]	No progression (N=79)[2]	Progression (N=30)[3]	No progression (N=79)[3]
Calories (Kcal/day)	1778 ± 623	1378 ± 406	1924 ± 553	1506 ± 715		
	p=0.0008		p=0.008			
Total fat (grams/ day)	76 ± 33	52 ± 23	82 ± 30	59 ± 39	61 ± 17	58 ± 20
	p=0.0002		p=0.0006		p=0.35	
Saturated fat	25 ± 12	17 ± 8	28 ± 11	20 ± 14	21 ± 7	19 ± 8

(grams/day)						
	p=0.0005		p=0.0007		p=0.32	
Unsaturated fat						
(grams/day)	44 ± 20	30 ± 13	47 ± 18	34 ± 23	35 ± 11	33 ± 13
	p=0.0002		p=0.0008		p=0.40	
Carbohydrates						
(grams/day)	208 ± 78	169 ± 57	223 ± 72	181 ± 94	176 ± 45	178 ± 54
	p=0.014		p=0.007		p=0.804	
Protein						
(grams/day)	73 ± 26	57 ± 21	80 ± 26	63 ± 34	62 ± 15	62 ± 18
	p=0.0054		p=0.0026		p=0.922	
	262 ± 125	213 ± 149	284 ± 174	232 ± 28	217 ± 172	228 ± 206
Cholesterol (mg/day)	p=0.168	p=0.168		p=0.75		
Linolenic acid						
(grams/day)	16 ± 8	10 ± 6	17 ± 7	11 ± 8	13 ± 5	11 ± 6
	p=0.0001		p<0.0001		p=0.03	
Oleic acid						
(grams/day)	27 ± 13	20 ± 9	30 ± 12	23 ± 16	22 ± 8	22 ± 10
	p=0.0034		p=0.0077		p=0.88	

1Crude (Mean ± Standard Deviation) consumption of the dietary factors stratified by AA progression

[2]Adjusted (Mean ± Standard Deviation) consumption of the dietary factors stratified by AA progression (adjusted for following medications: statin drug, antihypertensive medication, diabetic medication, anticoagulant and antiplatelet therapy)

[3]Adjusted (Mean ± Standard Deviation) consumption of the dietary factors stratified by AA progression (adjusted

for calories and following medications: Statins, antihypertensive, diabetic medications, anticoagulant and antiplatelet therapy)

Table 3: Distribution of unadjusted dietary factors among the different groups of stroke and TIA patients.

Discussion

Our results suggest that increased calorie intake is significantly associated with the progression of AA in stroke and TIA patients. The significant association between increased consumption of dietary fats and carbohydrates with AAA progression no longer remained significant after adjusting for the calorie intake. Major contributors to the calories in our study were carbohydrates and fats. This implies large meal constituting increased consumption of all the carbohydrates and fats contributed to increased calorie consumption which is associated with the progression of the AA. In our study dietary cholesterol was not related with the progression of AA.

Studies on aorta arch atheroma have shown the significant association of stroke and TIA. It is believed that atheroma serves as the nidus for the embolic phenomenon [2,3,7,8] and the casual association between aortic arch plaque and stroke was shown in Transcranial Doppler (TCD) studies measuring embolic signals [31] Furthermore, AA is a dynamic process, which undergoes both progression and regression. According to Sen et al., progression of the aortic plaque is associated with recurrent vascular events in stroke/TIA patients [10]. Iatrogenic embolization from aortic arch plaque and complications after catheterization are associated with severe aortic plaque detected by TEE [32]. Thus, aortic arch plaque is established as one of the potential significant risk factor for stroke [33]. Currently, there is no evidence based treatment approach that has been shown to be effective in treating and/or preventing AA formation and/or progression [34].

Multiple risk factors are involved in the development and progression of the AA and includes age, gender, heredity, hypertension, diabetes mellitus, hyperlipidemia, sedentary lifestyle, and smoking [13]. Furthermore, few studies have suggested that elevated levels of inflammatory markers and hyperhomocysteinemia as isolated risk factors for the development and progression of AA [11,17,18]. Several studies have investigated the effect of medications, specifically statins in arresting AA progression [22]. This is a novel study in an effort to elicit the role of dietary factors in the development and progression of the aortic atheroma. Coronary heart disease and stroke share several major risk factors and although prior studies have found a link between dietary fat and coronary heart disease, the association has been ambiguous in ischemic stroke. Long term Calorie restriction has been shown to be protective for the progression of atherosclerosis

[27-29]. According to Luigi Fontana et al., calorie restriction results in profound and sustained beneficial effects on the major atherosclerosis risk factors, serum Tchol, LDL-C, HDL-C, TG, and BP, that usually increase with advancing age [27]. Likewise, our results suggest that caloric restriction may result in beneficial effects on atherosclerosis and risk factors. Increased consumption of calories was associated with the progression of AA. High calorie intake contributed predominantly by carbohydrate and fat intakes was shown to be associated with the progression of atherosclerosis. This study shows high fat intake is associated with high calorie consumption, which is responsible for the progression of AA. Previous studies have not accounted for specific dietary factors adjusting for total calorie intake; therefore our findings challenge the traditional recommendation of reduced fat and cholesterol intake, without addressing total calorie intake.

Conclusion

We aimed to investigate the effect of dietary factors such as calorie intake and dietary fats on the progression of AA. Currently, there is still no sufficient evidence to suggest that dietary fat intake increases ones risk for ischemic stroke. However, it should not be mistaken that one does not need to monitor his or her dietary fat intake. The results of this study show an association of increased calorie intake with the progression of aortic arch in a subset of stroke patients. Major contributors to the total calories were carbohydrates and fats. Subsequently, diet modifications may be a crucial step in prevention of recurrent stroke due to embolic phenomenon from AA. As a means of preventing stroke, we should also consider dietary modifications in conjunction with lifestyle modifications such as regular exercise, smoking cessation, blood pressure management, and alcohol consumption in moderation.

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