

lower mortality from cerebral hemorrhage and infarction in the Hiroshima/Nagasaki study⁶⁰. A meta-analysis of eight European cohort studies showed that vegetable and fruit intake was associated with a reduced risk of stroke, and consumption of more than 5 servings of vegetables and fruits per day was recommended⁶¹.

Dairy calcium

As in Western populations, an inverse association has been found between dairy calcium intake and mortality from stroke. Japanese consumption of milk and other dairy products is far lower than in Western countries⁶²; however, a median calcium intake of 116 mg/day from dairy products, suggested to be contained in half a glass of milk, was associated with an approximately 30% lower ischemic stroke incidence⁶³, and a cup of milk providing dairy calcium (150 mg/day in men, 173 mg/day in women) reduced the mortality from hemorrhagic, ischemic and total stroke⁶⁴.

Soy and isoflavones

Higher consumptions of soy and soy products containing isoflavones (more than 5 days/week) is associated with prevention of cerebral infarction in women and this association was observed primarily among postmenopausal women⁴⁷.

Saturated fatty acids

Very low saturated fatty acid intake (5 g/day) was confirmed to be associated with an increased risk of intra-parenchymal hemorrhage after adjustment for the serum total cholesterol level⁶⁵. Another survey conducted between 1988 and 1990 (JACC Study) also indicated an inverse association of saturated fatty acid intake with mortality from total stroke, intra-parenchymal hemorrhage, and ischemic stroke, except from sub-arachnoid hemorrhage⁴⁶. Similar trends were reported in American women 34-59 years of age, whose saturated fatty acid intake was approximately 3 times that of their Japanese counterparts⁶⁶.

Fish and n-3 polyunsaturated fatty acids

There have been no prospective studies on the preventive effects of fish and fish oil on recurrence of stroke. Subanalysis of the JELIS trial, mentioned before, showed that the administration of highly purified EPA appeared to reduce the risk for recurrent stroke in Japanese with hypercholesterolemia taking a statin, but not the risk for primary prevention of stroke⁶⁷.

Ethanol

The association of heavy ethanol consumption with the incidence of stroke is different from the incidence of CAD. Compared with occasional drinkers, heavy drinkers, i.e. those consuming >450 g/week had a 1.5- to 2-fold higher risk of total and hemorrhagic stroke. Light to moderate alcohol consumption, i.e., 1 to 149 g/week (<2 drinks/day), does not raise the total stroke risk⁶⁸.

The Japan Diet

Based on the substantial evidence above, adequate control of total energy and SFA intake, sufficient consumption of fish, soybeans and soybean products, fruits and vegetables, folate and vitamin B6, as well as modest alcohol intake, are useful for the prevention of CAD. In addition, specific foods, such as seaweed, mushrooms, konnyaku (boiled paste made from the arum root), and burdock, containing a large amount of dietary fiber but few calories, are frequently consumed in Japan. Japanese tea is high in antioxidants. These factors may all contribute collectively to the prevention of CAD and are presumably contained in the Japan diet.

Traditional Japanese cuisine

The so-called Japan diet characterized by consuming the foods described above, cooking by traditional Japanese methods, attributable to spiritual dietary culture partly derived from Zen, could promote a balanced intake of various nutrients while minimizing excess energy intake. Staple foods such as grains are commonly boiled without oil. Fish and shellfish, meat and poultry, eggs, soybeans and soybean products are used as main dishes. Main and side dishes are usually raw, steamed, boiled, grilled, roasted, or pan-fried with minimal addition of plant oil, but not animal fat. Vegetables and soybean products are prepared as side dishes and bonito soup, made from dried fish, konbu seaweed and dried shiitake mushrooms, which enhance the umami taste and flavor of glutamic and inosinic acids, are used for taste good. Japanese tea consumed without sugar contributes to low energy intake. The Japanese traditional method of combining foods and preparing dishes is notable for protecting against CAD.

Conclusions and message for the future

Recently, changes in societal structure have affected many aspects of the Japanese lifestyle, including

dietary habits. Food distribution systems and individual attitudes regarding eating have changed and people are consuming more meals outside of their homes, readily procuring salty prepared foods. The Japanese dietary style has become westernized, a diversification which has resulted in an increase in subjects with atherosclerotic risks, such as obesity, dyslipidemia, and hyperinsulinemia with impaired glucose tolerance. This tendency is particularly marked in younger persons. As a typical example of increasing metabolic syndrome in Japan, inhabitants of Okinawa prefecture were formerly the most long-lived population in Japan, as was apparent after World War II. Their traditional eating habits are recognized as preventive methods against cardiovascular disease⁶⁹; however, the mean life expectancy among males in Okinawa has not increased since 1980 and has remained below the national average since 2000^{70, 71}. People living in Okinawa are recognized as having changed early to a North American lifestyle, relative to the rest of Japan. In the near future, the risk of atherosclerotic disorders among Japanese is anticipated to increase if this lifestyle trend continues. In addition, it is important to prevent the global spread of metabolic syndrome, a lifestyle-related disease. It must be recognized that awareness of health and changes in dietary habits are the most useful strategies for both primary and secondary prevention of CAD, as described elsewhere⁷²⁻⁷⁴. The Japanese population has traditionally consumed foods and nutrients effective for preventing CAD, and this diet has been readily available in our daily lives; however, as mentioned previously, increased rates of obesity, hypercholesterolemia, and impaired glucose tolerance in both genders may become a health problem for the next generation in Japan. A recent epidemiological study revealed that elevated intake of white rice is associated with an increased risk of type 2 diabetes in Japanese women and is suggestive of a positive association in men who were not engaged in strenuous physical activity⁷⁵. Although rice consumption has decreased during the past several decades, nearly 30% of total energy intake for Japanese is still derived from rice⁷³. The Japan diet described herein, including less refined carbohydrate intake, may provide a useful tool for preventing, or at least ameliorating, metabolic syndrome and related disorders.

These results suggest that the following strategies are useful for CAD and stroke prevention based on previous dietary changes in Japan: (1) a diet with adequate total calories, (2) increased intake of fish and plant foods, (3) decreased intake of refined carbohydrate and animal fat, (4) decreased intake of salt.

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Part-2

臨床栄養学

動脈硬化性疾患予防ガイドライン 2012年版を中心とした食事療法

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Keyword

食事療法, 動脈硬化性疾患予防ガイドライン, 冠動脈疾患, 脂質異常症, メタボリックシンドローム

はじめに

このたび、日本動脈硬化学会から新たな「動脈硬化性疾患予防ガイドライン2012年版」(以下、ガイドライン2012と略)¹⁾が発表された。ここでは、より多くのリスクを抱える症例を網羅的に把握するため、新たに境界域高LDLコレステロール血症(LDL-C:120~139mg/dl)という基準値が設置された。また、予防対象としての患者層別化において、NIPPON DATA80²⁾というわが国の疫学的成績から算出した絶対リスクをもって評価する手法が取り入れられ、動脈硬化性疾患の管理を脂質異常症、高血圧症、糖尿病、喫煙を中心に、メタボリックシンドローム、肥満症、慢性腎臓病(CKD)、高尿酸血症など、さまざまな危険因子も含めて包括的な立場で管理することの重要性が示された。そしてとりわけ、注目すべき高リスク病態として、冠動脈疾患既往者、耐糖能異常とは切り離れた糖尿病患者、家族性高コレステロール血症があげられ、CKDや脳血管障害、末梢動脈疾患(PAD)に対してもエビデンスの肉付けがなされた。また、血清トリグリセライド(TG)値が400mg/dlを超える症例や食後採血によりLDL-Cの算定・評価にFriedewaldの公式が適用されない症例に対する補助診断(二次的判断基準)としてNon-HDL-Cを用いる考え(Non-HDL-Cの基準値=LDL-Cの基準値+30mg/dl)が導入された。

冠動脈疾患(CAD)で代表される動脈硬化性疾患の一次、二次予防を達成するすべは表1にあげた危険因子を掌握し、その是正に努めることにある。とりわけ脂質異常症、糖尿病、耐糖能異常、高血圧などを早い時期から診断し治療につなげることは重要であり、安全性に配慮した治療方針の決定が望まれる。本稿で取りあげる食事療法は、こうした治療の先駆けとなるものであり、禁煙の推進とともに食事療法、運動療法を中心とした生活習慣の改善が主体となる。

食事療法の意義

食事療法を行うことにより、脂質異常症をはじめ、糖代謝異常、高血圧、肥満などのCADリスクの軽減や過酸化予防も合わせて達成され、用いるべき薬剤の減量が可能となる。

ガイドライン2012¹⁾では、これまでと同様に

表1 動脈硬化性疾患の危険因子

- ・高LDLコレステロール血症
- ・低HDLコレステロール血症
- ・加齢(男性 \geq 45歳, 女性 \geq 55歳)
- ・糖尿病
- ・高血圧
- ・喫煙
- ・冠動脈疾患(CAD)の既往
- ・高トリグリセライド血症
- ・家族歴
- ・メタボリックシンドローム
- ・慢性腎臓病(CKD)
- ・末梢動脈疾患(PAD), 非心原性脳梗塞
- ・耐糖能異常
- ・肥満
- ・A型性格, ストレス
- ・高尿酸血症

脂質異常症の治療の第一歩に生活習慣の改善をあげ、7項目の改善策(表2)を提示している。そのうえで、食事の管理方式について前回までの2段階食事療法の提示から、一挙に表3に示す基本的食事内容を指導に移す考え方が示された。こうしたことを基盤に LDL-C や血清 TG が高い場合、HDL-C が低い場合、それぞれの食事療法のあり方が記載され、脂質異常症の病型に沿った食事制限の強化を中心とした内容が用意された。また、メタボリックシンドローム、高血圧、糖尿病の食事についても簡便に記述された。全体を通じ強調されたことは、1日のコレステロール摂取量は300 mgではなく200 mg未満となり、炭水化物エネルギー比は55~60%から50~60%と下限値が訂正され、摂取食塩量は6 g/日未満を目標にすることなど指導開始当初から厳しい設定値

のもとでの管理を行うことの重要性である。

食事療法の有用性はすでに DASH 食³⁾、DASH-sodium 食⁴⁾、OmniHeart 食^{5,6)}、NCEP ステップ食⁷⁻⁹⁾、GISSI 食¹⁰⁾、地中海食^{11,12)}などで認められ、CAD 既往者を対象とした Lyon Diet Heart Study¹²⁾においては地中海食が従来食に比べてCAD 二次予防リスクを70%も低減した結果が得られている。そうしたなか、ガイドライン 2012 では、とりわけ日本食の有用性が強調された。Seven Countries Study^{13,14)}や Ni-Hon-San Study¹⁵⁾は食生活を中心にわが国の生活様式が効を奏し、わが国の食材を用いた伝統的な日本食¹⁶⁾がCAD 発症予防に有効であることを示している。そして、減塩に留意した日本食型の食パターンでは洋風型と比べてCAD 死発生が約20%低いとの報告¹⁷⁾が取りあげられている。

具体的な食事療法の内容

こうしたガイドラインの趣旨から栄養食事療法として3つの柱を考えてみる。その1つは減量を目的とした総摂取エネルギーの制限であり、第2として炭水化物(糖質)、脂質、たんぱく質といった三大栄養素の摂取割合を再調整し、それぞれの中身を工夫選択すること、さらに第3の柱として食行動を改善すること(表4)である。とくに食行動の把握は、各人の生活様式の中身が観察され、生活上の価値観、食事に対する関心度のバ

表2 動脈硬化性疾患予防のための生活習慣の改善

1. 禁煙し、受動喫煙を回避する
2. 過食を抑え、身体活動を増やして標準体重を維持する
3. 肉の脂身、乳脂肪、卵黄の摂取を抑え、魚類、大豆製品の摂取を増やす
4. 野菜、果物、未精製穀類、海藻の摂取を増やす
5. 食塩を多く含む食品の摂取を控える
6. アルコールの過剰摂取を控える
7. 有酸素運動を毎日30分以上行う

(日本動脈硬化学会、動脈硬化性疾患予防ガイドライン 2012 年版¹⁾より)

表3 動脈硬化性疾患予防のための食事

1. エネルギー摂取量と身体活動量を考慮して標準体重〔身長(m)²×22〕を維持する
2. 脂肪エネルギー比率を20~25%、飽和脂肪酸を4.5%以上7%未満、コレステロール摂取量を200 mg/日未満に抑える
3. n-3系多価不飽和脂肪酸の摂取を増やす
4. 炭水化物エネルギー比率を50~60%とし食物繊維の摂取を増やす
5. 食塩の摂取は6 g/日未満を目標にする
6. アルコール摂取を25 g/日以下に抑える

(日本動脈硬化学会、動脈硬化性疾患予防ガイドライン 2012 年版¹⁾より)

表4 脂質異常症改善のための食行動10カ条

1. 1日3食の配分をほぼ均等とし、定期的に食べる
2. 腹八分目を守る
3. 「早食い、ながら食い、まとめ食い」を避ける
4. 食物繊維を先に食べる
5. よくかんで食べる
6. まわりに食物を置かず、食環境のけじめをつける
7. 好きなものでも一人前までとして、適量を守る
8. 就寝前の2時間は重いものを食べない
9. 食器を小ぶりにする
10. 外食では丼物より定食物を選択

(日本動脈硬化学会、高脂血症治療ガイド 2004 年版より)

ロメーターともなり、行動変容を促す際の基準ともなる。

より具体的な食事療法では、血圧、血糖値に配慮しながら、脂質異常症の是正に努めることになる。その際、脂質異常症の病型に合わせた食事指導内容が求められる。CAD発症に関与する脂質異常症は家族性高コレステロール血症を代表とする高LDL-C血症と家族性複合型高脂血症、家族性Ⅲ型高脂血症、メタボリックシンドロームなどで出現する高TG血症＋低HDL-C血症に大別され、食事療法の位置づけや指導内容も異なる。高LDL-C血症では食事療法に対し抵抗例が多く、リスクの高い症例では食事指導とともに比較的早期（食事療法開始後3カ月程度）から薬物療法併用を考慮してよく、CAD既往者では食事指導とともに薬物療法を開始することも可能である。一方、高TG血症＋低HDL-C血症は食事療法や運動療法などが奏功するため、積極的な指導が望まれる。

●肥満対策

ガイドライン2012では肥満の目安としてBMI〔体重(Kg)／身長(m)²〕>25を設定し、さらに健康障害を合併するか合併が予想される場合には肥満症と診断するという日本肥満学会の診断基準¹⁸⁾を踏襲している。そして、メタボリックシンドロームの病態の中心的要因である内臓脂肪を減少させることは脂質異常症だけでなく、高血圧や耐糖能異常の改善が期待できることが示され、内臓肥満の日常診療におけるスクリーニング手段として臍高部ウエスト周囲長計測を用い、男性で85 cm以上、女性で90 cm以上の場合に内臓脂肪蓄積が疑われるとし、腹部CTスキャンを用いて臍高部の内臓脂肪面積を測定して100 cm²以上を内臓型肥満と定義している。

治療においては緩徐な肥満是正を推奨している。超低エネルギー食などを用いた短期間での体重減少は高率に体重のリバウンドを招く恐れがあり、かたや食事・運動療法による5%程度の肥満改善でも肥満に起因する比較的軽度な脂質・血

糖・血圧などの異常は、早期に改善されるからであるとしている。1 cmの腹囲の減少は約1 kgの体重減少と同等となり、体重あるいは臍高部ウエスト周囲長の5%減を3～6カ月間での目標とし、その達成度を経時的に評価することが重要であるとされる。

●高LDL-C血症に対する食事療法

LDL-C値はさまざまな食事性要因による修飾を受ける¹⁹⁾。実際、LDL-C変化量は摂取飽和脂肪酸(SFA)量、摂取トランス型不飽和脂肪酸(TFA)量ならびに摂取コレステロール量と正比例し、摂取多価不飽和脂肪酸(PUFA)量や摂取食物繊維量に反比例する。そして、総摂取エネルギーの増加は体重増加を介してLDL-C値を増加させる。

摂取するSFAをほかの栄養素に置換した際の血清脂質の変化をみると、炭水化物への置換ではLDL-C値は低下するが、同時にHDL-Cも低下するためLDL-C/HDL-C比は変化しない成績が多い。SFAを一価不飽和脂肪酸(MUFA)ならびにPUFAに置換した場合ではLDL-C値が低下する一方、HDL-Cはあまり変化しないためLDL-C/HDL-C比は低下する²⁰⁾。炭水化物摂取をTFAに等エネルギーで変換すると総コレステロール/HDL-C比は増加し、SFAに変換すると総コレステロール/HDL-C比は変わらず、MUFAやPUFAに変換すると総コレステロール/HDL-C比は低下する(図1)^{21, 22)}。なお、21件の前向きコホート研究をメタアナリシスした最近の成績²³⁾では、SFA摂取とCAD、脳血管障害のそれぞれ、ならびにこれら両者の発症リスクとの統計学的に有意な因果関係は見出せなかった。わが国のコホート研究の結果でもSFA摂取はCAD死発生との有意な関連性は認めず、SFAの最高摂取群(中間値20.3 g/日)では最低摂取群(中間値9.2 g/日)に比べ、脳卒中死発生、脳内出血発症、虚血性脳梗塞発症の相対危険率はいずれも有意に低く、SFA摂取増加は脳血管障害による死亡に対してむしろ抑制的に働いてい

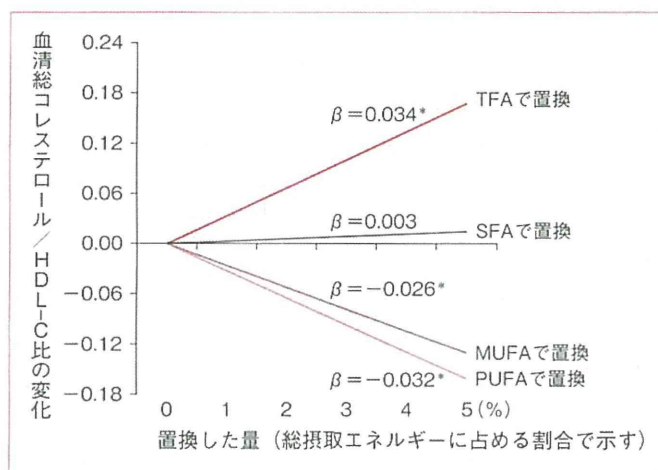


図1 炭水化物をさまざまな脂質に置換したときの血清総コレステロール/HDL-C比の変遷

トランス型脂肪酸 (TFA) で置換すると血清総コレステロール/HDL-C比は増加するが、一価不飽和脂肪酸 (MUFA) や多価不飽和脂肪酸 (PUFA) での置換では低下する。飽和脂肪酸 (SFA) では不変であった。

(Baum SJ, et al. J Clin Lipidol 2012; 6(3): 216-34²²⁾ より)

る²⁴⁾。SFA 摂取を減らして精製糖質や単純糖質 (単糖類や2糖類) に置き換えた場合²⁵⁾、マーガリンなどの TFA に置き換えた場合にはいずれも HDL-C や LDL 粒子サイズの低下、血清 TG の増加、さらに血糖値の増加を招き、こうした置換が CAD 発症を低下したとの成績はなく、むしろ増加する懸念もあると述べている。こうしたことを受け開催された CAD 予防のための SFA 摂取の評価を巡る専門家会議における見解では^{22, 26)}、SFA を PUFA 摂取に置換することで CAD リスクが減少することは疫学的、臨床的、ならびに体系的な研究からの一貫性のあるエビデンスであると結論付け (図 2)、1% の SFA を PUFA に置き換えることにより少なくとも 2~3% の CAD 発症を減少させるという報告²⁷⁾ を例示した。SFA や TFA には NF- κ B, Cox2, interleukin 6, TNF α などの炎症性サイトカインを活性化させる作用も報告され^{20, 28)}、やはり LDL-C 値が高い症例には置換する相手の栄養素を吟味した SFA 摂取制限が推奨されると結論された。

上述した TFA は、不飽和脂肪酸に水素添加して安定化させる際、不完全な水素抱合にて派生す

るトランス型の脂肪酸である。こうして工業的に生成された異性体である TFA (iTFA) は独特の風味を有し、劣化も少ないこともあり、これまで好んで食用とされてきた。しかし、Seven Countries Study では TFA 摂取と血清コレステロール値ならびに CAD 死発生の増加との関連性が指摘された²⁹⁾。実際、TFA は LDL-C を増加し、HDL-C を低下し、LDL-C/HDL-C 比を当量の SFA 摂取時の 2 倍近くにまで増加させる³⁰⁾。そのほか、前述した炎症性サイトカインを賦活化するほか、Lp(a) を増加すること、インスリン抵抗性を亢進し耐糖能を悪化させること、血管内皮機能を障害すること、必須脂肪酸代謝やプロスタグランジン代謝に悪影響を与えること、免疫力を低下し、クローン病との関連性があることや不妊症が多くなることなどが報告される。

食物繊維、とくに水溶性の食物繊維は LDL-C 低下作用をもつ。食物繊維には食事の量を確保し、満腹感を味わいながらも相対的に脂肪吸収を抑制し、摂取エネルギーや食後の血糖の上昇も低くする効用がある。食物繊維を充足するためには、未精製穀類 (玄米や大麦など)、大豆 (おか