https://doi.org/10.33805/2638-812X.110
Volume 3 Issue 1 | PDF 110 | Pages 3

EDELWEISS PUBLICATIONS
OPEN ACCESS

Journal of Obesity and Diabetes

Commentary ISSN: 2638-812X

The Influence of Unsaturated Fatty Acids for Atherosclerosis in Recent Years

Masahiro Bando[1] and Hiroshi Bando[2*]

Affiliation

[1]Department of Gastroenterology and Oncology, Institute of Biomedical Sciences, Tokushima University Graduate School, Japan
[2] Medical Research, Tokushima University, Japan
[*]**Corresponding author:** Hiroshi Bando, Medical Research, Tokushima University, Japan, Tel: +81-90-3187-2485, E-mail: pianomed@bronze.ocn.ne.jp

Citation: Bando M and Bando H. The influence of unsaturated fatty acids for atherosclerosis in recent years (2019) J Obesity and Diabetes 3:9-11

Received: Feb 28, 2019
Accepted: Apr 09, 2019
Published: Apr 12, 2019

Copyright: © 2019 Bando M et al., This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Keywords: Atherosclerosis, Unsaturated Fatty acids, Coronary heart disease, Diabetes.
Abbreviations: MUFA-Monounsaturated Fatty Acids, PUFA-Polyunsaturated Fatty Acids, EPA-Eicosapentaenoic Acid, JELIS-Japan EPA Lipid Intervention Study, ASCEND-Study of Cardiovascular Events in Diabetes, ORIGIN-Outcome Reduction with an Initial Glargine Intervention.

There have been various discussions of Monounsaturated Fatty Acids (MUFA) and Polyunsaturated Fatty Acids (PUFA) for influencing atherosclerosis. MUFA seems to have beneficial effects on the risk of coronary heart disease and atherosclerosis [1], and the authors have reported the marine-derived long-chain MUFA decrease atherosclerosis lesion development and total cholesterol in mouse [2]. On contrast, n-3 PUFA has been studied by GISSI-P trial, which was the Gruppo Italiano Per Lo Studio Della Sopravvivenza Nell'lnfarto Miocardio-Prevenzione (GISSI-P) Trial [3].

It included 11,324 subjects who had myocardial infarction followed up for 3.5 years. Administration of n-3 PUFA significantly lowered the risk of primary endpoint by 10%, suggesting beneficial effect statistically. Consecutive study showed the clinical effects for death, combined death, stroke and non-fatal myocardial infarction. Furthermore, it attributed the reduced risk of the events for overall by 20%, cardiovascular by 30%, and sudden death by 45% [4].

From historical aspect of lipids and atherosclerosis, there were observational studies concerning risk of heart disease and consumption of fish. They indicated the inverse relationship between heart disease and intake of fish [5]. After that, eating fish about 40-60g per day would be effective for the reducing cardiovascular mortality approximately half level. This amount is compatible for intake of about 0.2 to 1.0g of n-3 fatty acids [6].

Consecutively, there was a report by Japan EPA Lipid Intervention Study (JELIS) [7]. Subjects (n=18, 645) were assigned to receive either 1800mg of EPA with statin (EPA group) or statin only (control group) for 5 years. After treatment, LDL-C levels reduced 25% in both groups. In contrast, EPA group showed 19% of reduction of major coronary events compared with the control group. Thus, EPA seemed to prevent coronary events, especially non-fatal coronary events.

Thus, various researches have been found concerning intake of fatty food and particular types of vascular events such as heart failure, arrhythmia and coronary heart disease. Among them, there have been controversies as to the randomized trials of supplement with n-3 fatty element. A protocol was that supplement with a combination of EPA and DHA were provided for 40 months [8]. Further, continuous administration of n-3 fatty acids 1g/day was tried for 12,536 subjects for 6.2 years in average [9].

As the results, the rate of cardiovascular events was not decreased in patients at high risk. Furthermore, meta-analysis of 10 trials involving 77,917 individuals has performed [10]. In this analysis, there were not identified significant beneficial effects of n−3 fatty acid on major vascular events.

As to the guideline of American Heart Association (AHA), n-3 fatty acid supplements have been currently recommended for secondary prevention of coronary heart disease [11]. Similarly, n-3 fatty acid intake is also beneficial for primary prevention of cardiovascular disease [12].

In the clinical practice, blood lipid control has been continued for long [13]. Its purpose is to prevent arteriosclerotic diseases, such as coronary heart disease. As one of the intervention tests, the JELIS trial has been conducted in Japan, in which the effect of inhibiting cardiovascular events was studied by administration of eicosapentaenoic acid (EPA) [7].

Based on this result, the Japan Atherosclerosis Society (JAS) announced "Guidelines for Preventing Arteriosclerotic Diseases (2012 Edition)". In the guideline, it was judged that the effectiveness of EPA was confirmed. Furthermore, it was evaluated to be the recommendation level IIa (rather effective and utility), and evidence level A (data based on many RCT and meta-analysis).

Thereafter, re-evaluation was done from the results of various reports, and two important research papers were cited in the 2017 edition, which were Alpha Omega test [8] and ORIGIN (Outcome Reduction With An Initial Glargine Intervention) trial [9]. From these results, it was concluded as follows: In a recent large-scale clinical trial, the effect of inhibiting cardiovascular events by administration of n-3 (ω-3) PUFA could not be demonstrated."

Recently, some important papers have been published. Among them, results of a cardiovascular event inhibition test by n-3 PUFA were reported. Out of the results of three reports, two cases were unable to prove their effect, and one was found to be effective. These results will be meaningful for evaluating the effect of n-3 PUFA for the future prevention of arteriosclerotic diseases.

The first report is the ASCEND (A Study of Cardiovascular Events in Diabetes) test [13]. This is a RCT study comparing EPA/DHA and olive oil in diabetic patients by the Clinical Research Department of Oxford University in England. The group was divided into 4 groups by 2 randomizations. One randomization is the n-3 group [EPA 460 mg and DHA 380 mg] and the placebo group (matching olive oil). The other randomization is the aspirin group (aspirin 100 mg) and the placebo group.

The primary end point was 4 situations, including nonfatal myocardial infarction, stroke excluding cerebral hemorrhage, cardiovascular death excluding cerebral hemorrhage, and Transient Ischemic Attack (TIA). As a result, cardiovascular protective effect was not observed when 15,480 patients were followed for 7.4 years. Further, no difference was found between the two groups (rate ratio 0.97, P = 0.55) as a result of the main endpoint.

These results were compared the results of the JELIS trial [7] and the guidelines of the American Society of Cardiology [14]. The latter showed the secondary preventive effect of n-3 PUFA on cardiovascular disease [14]. According to these evidence and comparison, they concluded that there was no preventive effect for cardiovascular disease by n-3 PUFA administration. ASCEND test had also included the study of two groups whether aspirin was daily administrated or not [15].

The incidence of the main endpoint was significantly lower in the aspirin group (8.5% vs. 9.6%), but conversely the rate of onset for bleeding as an adverse effects was high (4.1% vs. 3.2%). This result suggested that evaluation and judgment should be considered carefully associated with various factors and their balance in both situations.

How should we consider these results? As a conventional evaluation, the GISSI-PREVENZIONE test had the effect of recurrence prevention [16], and the JELIS test had the effect of initial prevention [7]. Therefore, n-3 PUFA seemed to have preventive effect against cardiovascular disease [17] from multi-faceted action. Future task would be the problems of EPA alone, combined DHA/EPA, the influence of α-linolenic acid and others.

In contrast, recent clinical research seems to show a little different result as compared with before. There were unremarkable effect in the Alpha Omega test [8] and the Origin test [9]. Moreover, recent studies revealed no effectiveness in RCT blinding in meta-analysis [10]. The results showed that cardiovascular inhibitory effect was not significantly different between n-3 and control groups, from the viewpoint of non-fatal myocardial infarction, coronary artery disease death, and total coronary artery disease [10]. There is a meaningful report, which was the PREDIMED test in 2013 and also 2018 [18]. In this study, olive oil was administered to the control group. Three kinds of diets were:

i) Mediterranean diet with extra-virgin olive oil
ii) Mediterranean diet with mixed nuts, and
iii) Control diet with reduced dietary fat.

The results were that i) and ii) showed lower incidence of major cardiovascular events in the persons at high cardiovascular risk [18]. In summary, recent several reports shows that n-3 PUFA cannot always have clinical effects for arteriosclerotic diseases in primary and secondary prevention aspects. Consequently, further research in this field will be expected with the specific protocol to clarify detail relationships among lots of factors.

References

1. Joris PJ and Mensink RP. Role of cis-monounsaturated fatty acids in the prevention of coronary heart disease (2016) Curr Atheroscler Rep 18:38. https://doi.org/10.1007/s11883-016-0597-y
2. Yang ZH, Bando M, Sakurai T, Chen Y, Emma-Okon B, et al. Long-chain monounsaturated fatty acid-rich fish oil attenuates the development of atherosclerosis in mouse models (2016) Mol Nutr Food Res 60:2208-2218. https://doi.org/10.1002/mnfr.201600142
3. GISSI-Prevenzione Investigators (Gruppo Italiano Per Lo Studio Della Sopravvivenza Nell'infarto Miocardico). Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial (1999) Lancet 354:447-455. https://doi.org/10.1016/S0140-6736(99)07072-5
4. Marchioli R, Levantesi G, Macchia A, Maggioni AP, Marfisi RM, Silletta MG, et al. GISSI-Prevenzione Investigators. Antiarrhythmic mechanisms of n-3 PUFA and the results of the GISSI-Prevenzione trial (2005) J Membr Biol 206:117-128.
5. Kromhout D, Bosschieter EB and de Lezenne Coulander C. The inverse relation between fish consumption and 20-year mortality from coronary heart disease (1985) N Engl J Med 312:1205-1209. https://doi.org/10.1056/NEJM198505093121901
6. Kris-Etherton PM, Harris WS, Appel LJ. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease (2002) Circulation 106:2747-2757.
7. Yokoyama M, Origasa H, Matsuzaki M, Matsuzawa Y, Saito Y, et al. Effects of eicosapentaenoic acid on major coronary events in hyper cholesterolaemic patients (JELIS): a randomized open-label, blinded endpoint analysis (2007) Lancet 369:1090-1098. https://doi.org/10.1016/S0140-6736(07)60527-3
8. Kromhout D, Giltay EJ, Geleijnse JM and Alpha Omega Trial Group. n-3 fatty acids and cardiovascular events after myocardial infarction (2010) N Engl J Med 363:2015-2026. https://doi.org/10.1056/NEJMoa1003603
9. The ORIGIN Trial Investigators, Bosch J, Gerstein HC, Dagenais GR, Díaz R, et al. n-3 Fatty acids and cardiovascular outcomes in patients with dysglycemia (2012) N Engl J Med 367:309-318. https://doi.org/10.1056/NEJMoa1203859
10. Aung T, Halsey J, Kromhout D, Gerstein HC, Marchioli R, et al. Associations of omega-3 fatty acid supplement use with cardiovascular disease risks: meta-analysis of 10 trials involving 77 917 individuals (2018) JAMA Cardiol 3:225-234. https://doi.org/10.1001/jamacardio.2017.5205
11. Siscovick DS, Barringer TA, Fretts AM, Wu JH, Lichtenstein AH, et al. Omega-3 polyunsaturated fatty acid (fish oil) supplementation and the prevention of clinical cardiovascular disease: a science advisory from the American Heart Association (2017) Circulation 135:867-884. https://doi.org/10.1161/CIR.0000000000000482
12. Rimm EB, Appel LJ, Chiuve SE, Djoussé L, Engler MB, et al. Seafood long-chain n-3 polyunsaturated fatty acids and cardiovascular disease: a science advisory from the American Heart Association (2018) Circulation 138:35-47. https://doi.org/10.1161/CIR.0000000000000574

13. The ASCEND Study Collaborative Group, Bowman L, Mafham M, Wallendszus K, Stevens W, et al. Effects of n-3 Fatty Acid Supplements in Diabetes Mellitus (2018) N Engl J Med 379:1540-1550. https://doi.org/10.1056/NEJMoa1804989
14. Smith SC Jr, Benjamin EJ, Bonow RO, Braun LT, Creager MA et al. AHA/ACCF Secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease. Update: A guideline from the american heart association and american college of cardiology foundation (2011) Circulation 124:2458-2473. https://doi.org/10.1161/CIR.0b013e318235eb4d
15. ASCEND Study Collaborative Group, Bowman L, Mafham M, Wallendszus K, Stevens W, et al. Effects of aspirin for primary prevention in persons with diabetes mellitus (2018) N Engl J Med. 379:1529-1539. https://doi.org/10.1056/NEJMoa1804988
16. Marchioli R, Barzi F, Bomba E, Chieffo C, Di Gregorio D, et al. Early protection against sudden death by n-3 polyunsaturated fatty acids after myocardial infarction: time-course analysis of the results of the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI)-Prevenzione (2002) Circulation 105:1897-1903. https://doi.org/10.1161/01.CIR.0000014682.14181.F2
17. Saravanan P, Davidson NC, Schmidt EB and Calder PC Cardiovascular effects of marine omega-3 fatty acids (2010) Lancet 376:540-550. https://doi.org/10.1016/S0140-6736(10)60445-X
18. Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, et al. Primary prevention of cardiovascular disease with a mediterranean diet supplemented with extra-virgin olive oil or nuts (2018) N Engl J Med 379:1387-1389. https://doi.org/10.1056/NEJMoa1800389