ECRONICON OPEN ACCESS

EC CARDIOLOGY
Review Article

Cardiovascular Disease: Good Fats and Bad Fats

Mark Houston*

Associate Clinical Professor of Medicine, Vanderbilt University Medical School, Director, Hypertension Institute and Vascular Biology, Medical Director of Division of Human Nutrition, Saint Thomas Medical Group, Saint Thomas Hospital, Nashville, Tennessee, United States

***Corresponding Author:** Mark Houston, Associate Clinical Professor of Medicine, Vanderbilt University Medical School, Director, Hypertension Institute and Vascular Biology, Medical Director of Division of Human Nutrition, Saint Thomas Medical Group, Saint Thomas Hospital, Nashville, Tennessee, United States.

Received: March 13, 2018; **Published:** April 09, 2018

Abstract

Cardiovascular disease (CVD) remains the number one cause of morbidity and mortality in the United States, with an annual cost exceeding 300 billion USD. Optimal nutrition is the corner stone of lifestyle interventions to prevent and treat CHD. Numerous prospective nutrition clinical trials have shown dramatic reductions in the incidence of CHD with proper nutrition. However, the role of some dietary fats has remained controversial in this regard. Nutritional science and nutrigenomics research provide new insights in strategies to prevent and treat CHD. This article will review the role of omega 3 fatty acids, monounsaturated fatty acids, saturated fatty acids and trans fatty acids in the prevention and treatment of CVD, CHD and myocardial infarction (MI).

Keywords: *Cardiovascular Disease (CVD); Coronary Heart Disease (CHD); Myocardial Infarction (MI)*

Introduction

Cardiovascular disease (CVD) remains the number one cause of morbidity and mortality in the United States with an annual cost (direct and indirect) of $320 billion USD [1,2]. There are over 2200 US citizens that die from stroke or MI daily [2-5]. Approximately 80% of CHD can be prevented by optimal nutrition, regular aerobic and resistance exercise, maintenance of ideal body weight and body composition, mild alcohol intake and avoidance of all tobacco products [1]. However, the role of some dietary fats in the prevention and treatment of CHD has remained controversial. This short review will examine the role of omega 3 fatty acids (OMFA), monounsaturated fatty acids (MUFA), saturated fatty acids (SFA) and trans fatty acids (TFA) in the prevention and treatment of CVD, CHD and myocardial infarction (MI).

Omega 3 Fatty Acids

The role of fats in CHD has been evaluated in numerous clinical trials [6-52]. A large meta-analysis of 18 RCTs (93,000 subjects) and 16 prospective cohort studies (732,000 subjects examined EPA+DHA (eicosapentaenoic acid and docosahexaenoic acid) from foods or supplements and the relationship to CHD, MI, sudden cardiac death, coronary death and angina in primary and secondary prevention [9]. Among RCTs, there was a non-statistically significant 6% reduction in CHD risk with EPA+DHA. Subgroup analyses of data from RCTs indicated a statistically significant 14% to 16% CHD risk reduction with EPA+DHA among higher-risk populations including with elevated triglyceride levels over 150 mg/dL and low-density lipoprotein cholesterol above 130 mg/dL. Meta-analysis of data from prospective cohort studies resulted an 18% significant reduction of CHD for higher intakes of EPA+DHA over one gram per day and risk of any CHD event. The sudden cardiac death (SCD) rate was reduced 47%. The greatest reduction in CHD (25%) occurred in those with high TG over 150 mg/dL and doses of omega 3 FA over one gram per day. These results and others indicate that EPA+DHA may be associated with a reduction in CHD risk, with the greatest benefit observed among higher-risk populations in RCTs and those taking higher doses of EPA and DHA. Omega 3 FA reduce ventricular arrhythmias [38] and decrease cardiovascular and total mortality [39]. Omega 3 FA are typically

found in cold water fish such as salmon, mackerel and others as well as plant-based products like algae, flax, chia, and hemp seeds, but as fatty fish eat algae, they serve as a supply for these essential fats. Omega 3 fatty acids decrease MI and CHD 18% more with concomitant use of statins [42], reduce stent restenosis [40], reduce post MI mortality [43] coronary artery bypass graft (CABG occlusion) [44,45], plaque formation [46,47], coronary artery calcification, [46,47] atherosclerosis [46,47], improve the lipid profile [48], lower glucose, improve insulin resistance [49-51] and reduce blood pressure [2,4,52]. The dose prescribed will depend on the condition being treated as well as age, body weight and use of concomitant medications and other nutritional supplements. It is best to use a balanced formulation with DHA, EPA, GLA and gamma-delta tocopherols. This will prevent oxidation in the cell membranes and reduce depletions of the EPA and DHA by GLA or vice versa [48,52].

Monounsaturated Fats

The effects of cis-monounsaturated fatty acids (cis-MUFAs) on the risk of CHD) and on CHD mortality have not been firmly established [53]. In addition, dietary recommendations for cis-MUFA from various organizations do not agree. The effects of cis-MUFA on serum lipids, lipoproteins and endothelial vascular function are favorable [29,53,54]. There are no randomized controlled trials with CHD events as endpoints but several large prospective cohort studies have been published on the relationship between cis-MUFA, extra virgin olive oil (EVOO) and nuts, and CHD risk [22,27,29,31,54,55]. Partial replacement of SFA with MUFA improves the blood lipid and lipoprotein profile and reduces the risk of CHD [29].

The Nurses' Health Study and the Health Professionals Follow-up Study followed over 84,000 patients for 24 to 30 years [31]. Replacing 5% of energy from SFA with equivalent energy intake from MUFA was associated with a 15% lower risk of CHD, HR: 0.85, 95% CI: 0.74 to 0.97; p = 0.02) [31]. Isocaloric replacement of 1% energy from 12:0-18:0 SFA combined showed a HR of CHD for MUFA of 0.94 (0.91 to 0.97; P<0.001) and for 16:0 the HR was .90 (0.83 to 0.97; P= 0.01) [22]. A recent review of the literature of randomized controlled clinical trials that used a 4-step cost-of-illness analysis estimated the success rate, disease biomarker reduction, disease incidence reduction and cost savings of incorporating MUFA into the diet [54]. Improvements were seen in CHD biomarkers incidence of CHD and T2 DM, in addition to annualized healthcare and societal cost savings for the daily MUFA intake [54].

In a prospective study of Dutch patients with cardiac disease (Alpha Omega Cohort) [55], the risk of CVD and CHD mortality was evaluated over 7 years and the sum of SFAs and TFAs was theoretically replaced by PUFAs or cis MUFAs in a group of drug-treated patients with a history of myocardial infarction. In continuous analyses, replacement of SFAs and TFAs with MUFAs (per 5% of energy) was associated with significantly lower risks of CVD mortality (HR 0.75) and CHD mortality (HR 0.70) [55]. Nutrition guidelines for dietary fats are now shifting to recommend higher intakes of MUFA such as EVOO and nuts [27,29,53-55].

Saturated Fatty Acids

Clinical trials offer conflicting conclusions regarding the role of SFA in the risk of CHD. This has led to confusion in the lay public that is exacerbated by recently published national best sellers and conflicting nutrition recommendations by national and international committees [6,10-37]. The source of the confusion lies within the complexity, accuracy and the coordination of the results and conclusions in basic science, clinical epidemiology and prospective clinical trials. Some of the misconceptions and improper interpretations are related to the source of the SFA, carbon length absorption, the replacement nutrient(s), the genotypic expression to dietary SFAs, metabolism and the composition and chemical expressions within the microbiome [10-14].

SFA also have variable effects on serum lipids and lipid subfractions, hepatic LDL receptor activity, nonalcoholic liver disease (NAFLD), thrombosis, release of tissue plasminogen activator, macrophage foam cell formation and growth, toll- like receptors (TLR 2 and TLR 4) interactions, nuclear factor (NF-kB) cytokine gene expression, NADPH oxidase, detoxification of radical oxygen species (ROS), activity of catalase, glutathione peroxidase (GPx), superoxide dismutase (SOD 1), thioredoxin reductase (TxNRD1) and the genetic ability to desaturate SFA to monounsaturated fatty acids. (MUFA) [10-20] Stearate (C-18) has minimal effect on CHD risk or serum lipids due to its rapid desaturation to MUFA by stearoyl-CoA Δ-9-desaturase (SCD), which is genetically determined [10-12]. The dietary SFA intake

may not correlate with the measured SFA content in serum cholesterol esters and erythrocytes, resulting in a discrepancy in the ability to accurately predict CHD risk based on the "real" SFA status of an individual [10,15-17]. High SFA content in serum cholesterol esters and erythrocytes, not high SFA intake, more accurately predicts CHD risk [15]. Endogenous SFA synthesis, especially that of palmitic acid (16:0) from carbohydrates, contributes to the SFA status. Increased dietary intake of refined carbohydrates with low dietary consumption of SFA spares SFA due to the de novo synthesis of SFA from refined carbohydrate. A diet with reduced carbohydrate intake allows SFA to be utilized directly for energy production. Long chain fatty acids (LCFA) enhance gastrointestinal growth of gram negative bacteria (GNB) and lipopolysaccharide (LPS) uptake, inflammation and immune activation of T-cells which will increase gastrointestinal permeability, the risk of endotoxemia and infection from a variety of pathobionts at a dysfunctional microbial-epithelial interface [10,15-19].

Published clinical trials and reviews have provided more accurate insights into the relationship of SFA and CHD [6,21-28]. A meta-analysis of 32 trials with over 600,000 subjects which included 17 observational studies of fatty acid (FA) biomarkers, 32 observational studies of FA intake and 27 randomized controlled clinical trials (RCCT) of FA supplementation [6]. The results of this meta-analysis is at variance with other studies perhaps due to the heterogenicity of the populations, selection bias, quality of studies selected, self -reporting of diet and other confounders due to unmeasured dietary factors and other lifestyle factors. Despite the size of this meta-analysis, the results and conclusions drawn need to be interpreted with caution.

The largest meta-analysis of three large cohort studies [Health Professionals Follow-Up Study (HPFS), the Nurses' Health Study (NHS 1) and the NHS-2] utilizing a 5% isocaloric (ISC) energy replacement of SFA with polyunsaturated fatty acids(PUFA) or vegetable fat, was associated with a 24% and 10% reduction in CHD risk, respectively [22]. The reduction in CHD with ISC energy replacement of SFA with PUFA, monounsaturated (MUFA), trans fatty acids (TFA), omega- 6 FA, whole grains, vegetable or plant proteins, refined carbohydrates, high fructose corn syrup or starches depends on the percent of energy that is substituted [22,23]. Replacement of 1% of energy from SFAs with PUFAs lowers LDL cholesterol which predicts a 2 - 8% reduction in CHD [22].

SFA intake and CHD were positively associated in the prospective, longitudinal cohort studies of over 115,000 men and women in the HPFS and the NHS over a 34 to 38- year follow-up [23]. SFAs were mostly lauric acid (12:0), myristic acid (14:0), palmitic acid (16:0), and stearic acid (18:0) at 9.0-11.3% of energy intake. Comparing the highest versus the lowest groups of individual SFA intakes, CHD increased 7% for 12:0, 13% for 14:0, 18% for 16:0, 18% for 18:0, and 18% for all four SFAs combined ($p = 0.05$ to 0.001]. The reduction in CHD after 1% energy ISC replacement of SFA 12:0-18:0 was 8% for PUFA, 5% for MUFA, 6% for whole grains and 7% for plant proteins [24].

The PREvención con DIeta MEDiterránea (PREDIMED) was a six -year prospective study of 7038 subjects with a high CVD risk that included MI, CVA or death from CV causes [27]. The dietary consumption of SFA and TFA from the highest to the lowest quintiles increased overall CVD by 81% and 67% respectively. The intake of PUFAs and MUFAs reduced the risk of CVD and death. The ISC replacement of SFAs or TFA with MUFAs and PUFAs reduced CVD [27]. SFA from processed foods increased CVD [27].

Conclusions and Summary on SFA [10-37]

SFA are diverse compounds cannot be "lumped" into a single category and have variable effects on CHD. It is prudent to replace long chain fatty acids (LCFA) with PUFA, MUFA, short chain fatty acids (SCFA), whole grains, plant proteins and perhaps medium chain fatty acids (MCFA). The daily recommended grams per day or percent of SFA relative to total fat or total calories cannot be accurately determined at this time. Some studies suggest that the SFA dietary intake should be well below 9% of the total caloric intake. The overall relationship of the human diet to CHD should include the totality of our nutrition and avoid reductionist evaluations of single macronutrients. New nutritional guidelines should promote dietary patterns that improve CHD based on validated science. Refined carbohydrates, high fructose corn syrup, starches and TFA increase the risk of CHD. Omega 6- FA appear to be neutral or improve CHD risk, whereas omega 3 FA(PUFA), MUFA, fermented foods, fiber, fruits and vegetables and the PREDIMED diet reduce CHD and CVD.

Conclusions regarding SFA and CHD

1. Dietary SFA intake is associated with an increased CHD risk and reducing dietary SFA in isocaloric (ISC) replacement with PUFA, MUFA, omega 6 FA, whole grains and plant proteins decrease CHD risk.
2. The source of the SFA is associated with the risk for CHD. Dietary intake of meat and animal fat have the greatest risk with a range of 6-48%.
3. LCFA are the most likely SFA associated with CHD risk. SCFA are not associated with CHD risk but additional studies are needed to confirm this.
4. Replacement of SFA with PUFA reduces CHD risk.
5. Replacement of SFA with MUFA reduces CHD risk
6. Replacement of SFA with omega 6 FA decreases CHD risk.
7. Replacement of SFA with refined CHO increases CHD risk.

Trans Fatty Acids

A study of 126,233 participants from the NHS and the HPFS analyzed the relationship between choices of dietary fats and overall mortality [56]. During the follow-up, 33,304 deaths were documented. Dietary TFA had the most significant adverse impact on health. Every 2% higher intake of TFA was associated with a 16% higher chance of premature death and a 25% increase in CHD death and nonfatal MI during the study period [56]. A panel of experts in cardiovascular nutrition recently reported on trending controversies and provided some recommendations regarding fat intake [57,58]. The overall recommendations were to reduce omega 6 fatty acids, increase omega 3 fatty acids and the ratio of omega 3 to omega 6 fatty acids and reduce SFA in addition to the elimination of TFA. The cardiovascular adverse effects of industrialized produced TFAs are shown below:

1. Dyslipidemia
    a. Increase TC: 8%
    b. Increase LDL-C: 9%
    c. Increase TG and VLDL: 9%
    d. Lower HDL-C: 2 - 3%
    e. Increase TC/HDL ratio: 11%
    f. Increase apolipoprotein B: 8%
    g. Increase lipoprotein (a) [Lp(a)]: 4%
2. Increase in adipose tissue TFA levels
3. Increase in TG and phospholipid TFA levels
4. Increase insulin resistance, glucose and T2DM risk
5. Increase thrombogenic risk and plaque vulnerability
6. Increase risk of CHD and MI
7. Increase risk of primary cardiac arrhythmias and sudden death
8. Increase in all -cause mortality by 25% from lowest to highest quintile
9. Increase of 2% in energy in total TFA intake results in 25% increase in CHD (CHD death and nonfatal MI)
10. Hypertension
11. Endothelial Dysfunction
12. Obesity
13. Increased inflammation

Coconut Oil

Coconut oil has been inappropriately promoted for a reduction in CHD and other CV events with no evidence to support it in human clinical trials. In a meta-analysis of 21 studies with 8 clinical trials and 13 observational studies, coconut oil increased TC and LDL more than PUFA, but less than butter, increased HDL and increased TG with no change in TC/HDL ratio. There was no change in CV events [59,60]. Coconut oil is 92% SFA, mostly lauric acid C12:0 (MCFA) and myrisitc acid (C14:0) which acts mostly like a LCFA. MCFA have rapid absorption, hepatic uptake and immediate oxidation for energy production. Both lauric and myristic acid increase LDL-C similar to other MCFA and LCFA,, but increase HDL-C more [61]. MCT (medium chain triglycerides) which are C-10 or less have direct portal vein absorption and are more water soluble. Only 4% of coconut oil is MCT of C-10 or less fatty acids. Coconut oil should not be recommended at this time for prevention or treatment of CHD or CVD due to the lack of prospective studies on CV outcomes, the mixed effects on serum lipids, the content of LCFA and the fact that replacement of coconut oil with PUFA and MUFA reduces CHD risk.

Conclusions

Omega 3 fatty acids reduce the risk of CHD, especially in higher risk patients and those taking higher doses of EPA and DHA. Monounsaturated fatty acids probably reduce CHD but more robust studies are needed to confirm this association as well as the patient subtypes which would benefit the most. Some LCFA increase the risk of CHD, but the SCFA do not increase the risk of CHD. All trans fatty acids increase the risk of CHD. Coconut oil has no proven benefit for CHD, but the primary constituents are LCFA which may increase CHD risk. It is recommended that dietary and supplement intake of omega 3 FA and MUFA be increased and the intake of LCFA be limited and trans fatty acids should be completely avoided.

Bibliography

1. Yusuf S., *et al.* "Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. INTERHEART Study Investigators". *Lancet* 364.9438 (2004): 937-952.

2. Houston Mark C. "What Your Doctor May Not Tell You About Heart Disease. The Revolutionary Book that Reveals the Truth Behind Coronary Illnesses and How You Can Fight Them. Grand Central Life and Style". Hachette Book Group. 237 Park Ave. New York, New York (2012).

3. O'Donnell CJ and Nabel EG. "Genomics of cardiovascular disease". *The New England Journal of Medicine* 365.22 (2011): 2098-2109.

4. Houston MC. "Nutrition and nutraceutical supplements in the treatment of hypertension". *Expert Review of Cardiovascular Therapy* 8.6 (2010): 821-833.

5. ACCORD Study Group., *et al.* "Long-term effects of intensive glucose lowering on cardiovascular outcomes". *New England Journal of Medicine* 364.9 (2011): 818-828.

6. Chowdhury R., *et al.* "Association of dietary, circulating, and supplement fatty acids with coronary risk: a systematic review and meta-analysis". *Annals of Internal Medicine* 160.6 (2014): 398-406.

7. Guasch-Ferré M., *et al.* "Dietary fat intake and risk of cardiovascular disease and all-cause mortality in a population at high risk of cardiovascular disease". *American Journal of Clinical Nutrition* 102.6 (2015): 1563-1573.

8. Ravnskov U., *et al.* "The questionable benefits of exchanging saturated fat with polyunsaturated fat". *Mayo Clinic Proceedings* 89.4 (2014): 451-453.

9. Alexander DD., *et al.* "A Meta-Analysis of Randomized Controlled Trials and Prospective Cohort Studies of Eicosapentaenoic and Docosahexaenoic Long-Chain Omega-3 Fatty Acids and Coronary Heart Disease Risk". *Mayo Clinic Proceedings* 92.1 (2017): 15-29.

10. DiNicolantonio JJ., *et al.* "The Evidence for Saturated Fat and for Sugar Related to Coronary Heart Disease". *Progress in Cardiovascular Diseases* 58.5 (2016): 464-472.

11. Siri-Tarino PW and Krauss RM. "Diet, lipids, and cardiovascular disease". *Current Opinion in Lipidology* 27.4 (2016): 323-328.

12. Adamson S and Leitinger N. "Phenotypic modulation of macrophages in response to plaque lipids". *Current Opinion in Lipidology* 22.5 (2011): 335-342.

13. Dow CA., *et al*. "Influence of dietary saturated fat intake on endothelial fibrinolytic capacity in adults". *American Journal of Cardiology* 114.5 (2014): 783-788.

14. Santos S., *et al.* "Systematic review of saturated fatty acids on inflammation and circulating levels of adipokines". *Nutrition Research* 33.9 (2013): 687-695.

15. Ruiz-Núñez B., *et al.* "Saturated fatty acid (SFA) status and SFA intake exhibit different relations with serum total cholesterol and lipoprotein cholesterol: a mechanistic explanation centered around lifestyle-induced low-grade inflammation". *Journal of Nutritional Biochemistry* 25.3 (2013): 304-312.

16. Forsythe CE., *et al*. "Comparison of low fat and low carbohydrate diets on circulating fatty acid composition and markers of inflammation". *Lipids* 43.1 (2008): 65-77.

17. Volek JS., *et al.* "Dietary carbohydrate restriction induces a unique metabolic state positively affecting atherogenic dyslipidemia, fatty acid partitioning, and metabolic syndrome". *Progress in Lipid Research* 47.5 (2008): 307-318.

18. Peña-Orihuela P., *et al.* "Antioxidant system response is modified by dietary fat in adipose tissue of metabolic syndrome patients". *Journal of Nutritional Biochemistry* 24.10 (2013): 1717-1723.

19. Devkota S., *et al.* "Dietary-fat-induced taurocholic acid promotes pathobiont expansion and colitis in Il10-/- mice". *Nature* 487.7405 (2012): 104-108.

20. Ma W., *et al.* "Prospective association of fatty acids in the de novo lipogenesis pathway with risk of type 2 diabetes: the Cardiovascular Health Study". *American Journal of Clinical Nutrition* 101.1 (2015): 153-163.

21. Praagman J., *et al.* "The association between dietary saturated fatty acids and ischemic heart disease depends on the type and source of fatty acid in the European Prospective Investigation into Cancer and Nutrition-Netherlands cohort". *American Journal of Clinical Nutrition* 103.2 (2016): 356-365.

22. Chen M., *et al.* "Dairy fat and risk of cardiovascular disease in 3 cohorts of US adults". *American Journal of Clinical Nutrition* 104.5 (2016): 1209-1217.

23. Zong G., *et al.* "Intake of individual saturated fatty acids and risk of coronary heart disease in US men and women: two prospective longitudinal cohort studies". *BMJ* 355 (2016): i5796.

24. Micha R and Mozaffarian D. "Saturated fat and cardiometabolic risk factors, coronary heart disease, stroke, and diabetes: a fresh look at the evidence". *Lipids* 45.10 (2010): 893-905.

25. de Souza RJ., *et al.* "Intake of saturated and trans unsaturated fatty acids and risk of all-cause mortality, cardiovascular disease, and type 2 diabetes: systematic review and meta-analysis of observational studies". *BMJ* 351 (2015): h3978.

26. Ruiz-Núñez B., *et al.* "The relation of saturated fatty acids with low-grade inflammation and cardiovascular disease". *Journal of Nutritional Biochemistry* 36 (2016): 1-20.

27. Guasch-Ferré M., *et al*. "Study Investigators Dietary fat intake and risk of cardiovascular disease and all-cause mortality in a population at high risk of cardiovascular disease". Am J Clin Nutr. 2015 102(6): 1563-73.

28. Chang LF., *et al.* "Adverse effects on insulin secretion of replacing saturated fat with refined carbohydrate but not with monounsaturated fat: A randomized controlled trial in centrally obese subjects". *Journal of Clinical Lipidology* 10.6 (2016): 1431-1441.

29. Zock PL., *et al.* "Progressing Insights into the Role of Dietary Fats in the Prevention of Cardiovascular Disease". *Current Cardiology Reports* 18.11 (2016): 111.

30. Ros E., *et al*. "Consensus On Fats And Oils In The Diet Of S Ish Adults Position Paper Of The Spanish Federation Of Food, Nutrition And Dietetics Societies". *Nutricion Hospitalaria* 132.2 (2015): 435-477.

31. Li Y., *et al.* "Saturated Fats Compared with Unsaturated Fats and Sources of Carbohydrates in Relation to Risk of Coronary Heart Disease: A Prospective Cohort Study". *Journal of the American College of Cardiology* 66.14 (2015): 1538-1548.

32. CFlock MR and Kris-Etherton PM. "Diverse physiological effects of long-chain saturated fatty acids: implications for cardiovascular disease". *Current Opinion in Clinical Nutrition & Metabolic Care* 16.2 (2013): 133-140.

33. Hooper L., *et al*. "Reduced or modified dietary fat for preventing cardiovascular disease". *Sao Paulo Medical Journal* 134.2 (2016): 182-183.

34. Andrew M., *et al.* "Trending Cardiovascular Nutrition Controversies" *Journal of the American College of Cardiology* 69. 9 (2017).

35. Björck L., *et al*. "Changes in Dietary Fat Intake and Projections for Coronary Heart Disease Mortality in Sweden: A Simulation Study". *PLoSOne* 11.8 (2016): e0160474.

36. Williams CM and Salter A. "Saturated fatty acids and coronary heart disease risk: the debate goes on". *Current Opinion in Clinical Nutrition & Metabolic Care* 19.2 (2016): 97-102

37. Dawczynski C. "Saturated fatty acids are not off the hook". *Nutrition, Metabolism & Cardiovascular Diseases* 25.12 (2015): 1071-1078.

38. Finzi AA., *et al.* "Effects of n-3 polyunsaturated fatty acids on malignant ventricular arrhythmias in patients with chronic heart failure and implantable cardioverter-defibrillators: A substudy of the Gruppo Italiano per lo Studio della Sopravvivenza nell'Insufficienza Cardiaca (GISSI-HF) trial". *American Heart Journal* 161.2 (2011): 338-343.

39. Mozaffarian D. "Plasma phospholipid long-chain ω-3 fatty acids and total and cause-specific mortality in older adults: a cohort study". *Annals of Internal Medicine* 158.7 (2013): 515-525.

40. Gajos G., *et al.* "Reduced thrombin formation and altered fibrin clot properties induced by polyunsaturated omega-3 fatty acids on top of dual antiplatelet therapy in patients undergoing percutaneous coronary intervention (OMEGA-PCI clot)". *Arteriosclerosis, Thrombosis, and Vascular Biology* 31.7 (2011): 1696-1702.

41. Davis W., *et al*. "Effect of a combined therapeutic approach of intensive lipid management, omega-3 fatty acid supplementation, and increased serum 25 (OH) vitamin D on coronary calcium scores in asymptomatic adults". *American Journal of Therapeutics* 16.4 (2009): 326-332.

42. Nozue T., *et al.* "Effects of serum n-3 to n-6 polyunsaturated fatty acids ratios on coronary atherosclerosis in statin-treated patients with coronary artery disease". *American Journal of Cardiology* 111.1 (2013): 6-11.

43. Greene SJ., *et al.* "Effects of Polyunsaturated Fatty Acid Treatment on Postdischarge Outcomes After Acute Myocardial Infarction". *American Journal of Cardiology* 117.3 (2016): 340-346.

44. Arnesen H. "n-3 fatty acids and revascularization procedures". *Lipids* 36 (2001): S103-S106.

45. Arnesen H and Seljeflot I. "Studies on very long chain marine n-3 fatty acids in patients with atherosclerotic heart disease with special focus on mechanisms, dosage and formulas of supplementation". *Cellular and Molecular Biology* 56.1 (2010): 18-27.

46. Sekikawa A., *et al.* "Long chain n-3 polyunsaturated fatty acids and incidence rate of coronary artery calcification in Japanese men in Japan and white men in the USA: population based prospective cohort study". *Heart* 100.7 (2014): 569-573.

47. Abedin M., *et al.* "N-3 fatty acids inhibit vascular calcification via the p38-mitogen-activated protein kinase and peroxisome proliferator-activated receptor-gamma pathways". *Circulation Research* 98.6 (2006): 727-729.

48. Jacobson TA., *et al.* "Effects of eicosapentaenoic acid and docosahexaenoic acid on low-density lipoprotein cholesterol and other lipids: a review". *Journal of Clinical Lipidology* 6.1 (2012): 5-18.

49. Jans A., *et al*. "PUFAs acutely affect triacylglycerol-derived skeletal muscle fatty acid uptake and increase postprandial insulin sensitivity". *American Journal of Clinical Nutrition* 95.4 (2012): 825-836.

50. García-López S., *et al*. "One month of omega-3 fatty acid supplementation improves lipid profiles, glucose levels and blood pressure in overweight schoolchildren with metabolic syndrome". *Journal of Pediatric Endocrinology and Metabolism* 29.10 (2016): 1143-1150.

51. Sawada T., *et al.* "Effects of 6-month eicosapentaenoic acid treatment on postprandial hyperglycemia, hyperlipidemia, insulin secretion ability, and concomitant endothelial dysfunction among newly-diagnosed impaired glucose metabolism patients with coronary artery disease. An open label, single blinded, prospective randomized controlled trial". *Cardiovascular Diabetology* 15.1 (2016): 1.

52. Houston M. "The role of nutrition and nutraceutical supplements in the treatment of hypertension". *World Journal of Cardiology* 6.2 (2014): 38-66.

53. Joris PJ and Mensink RP. "Role of cis-Monounsaturated Fatty Acids in the Prevention of Coronary Heart Disease". *Current Atherosclerosis Reports* 18.7 (2016): 38.

54. Abdullah MM., *et al.* "Health benefits and evaluation of healthcare cost savings if oils rich in monounsaturated fatty acids were substituted for conventional dietary oils in the United States". *Nutrition Reviews* (2017).

55. Mölenberg FJ., *et al*. "Dietary fatty acid intake after myocardial infarction: a theoretical substitution analysis of the Alpha Omega Cohort". *American Journal of Clinical Nutrition* 106.3 (2017): 895-901.

56. Wand DD., *et al.* "Specific Dietary Fats in Relation to Total and Cause-Specific Mortality". *JAMA Internal Medicine* 176.8 (2016): 1134-1145.

57. Trumbo PR and Shimakawa T. "Tolerable upper intake levels for trans fat, saturated fat, and cholesterol". *Nutrition Reviews* 69.5 (2011): 270-278.

58. Nestel P. "Trans fatty acids: are its cardiovascular risks fully appreciated?" *Clinical Therapeutics* 36.3 (2014): 315-321.

59. Eyres L., *et al.* "Coconut oil consumption and cardiovascular risk factors in humans". *Nutrition Reviews* 74.4 (2016): 267-280.

60. DeLany JP., *et al.* "Differential oxidation of individual dietary fatty acids in humans". *American Journal of Clinical Nutrition* 72.4 (2000): 905-911.

61. Feranil AB., *et al.* "Coconut oil is associated with a beneficial lipid profile in pre-menopausal women in the Philippines". *Asia Pacific Journal of Clinical Nutrition* 20.2 (2011): 190-195.

Volume 5 Issue 5 May 2018