Nutritional impact of micronutrients on cardiovascular diseases
Preface

In the western industrialized countries cardiovascular diseases are still the number 1 cause of death. Risk factors for cardiovascular diseases primarily include overweight, lack of physical exercise, smoking, hypertension, diabetes, psychosocial factors, increased lipid and homocysteine levels. Quite a number of micronutrients may improve the function of heart and blood vessels, which are omega-3 fatty acids, B vitamins, antioxidants, magnesium and various trace elements, etc.

Phytonutrients, such as mixed carotenoids and oligomeric proanthocyanidins from grape seeds, are strong radical scavengers which protect the vessels against arteriosclerosis. Polyphenols from grapes and cocoa support the vascular function and coenzyme Q$_{10}$ as well as L-carnitine are essentially involved in the energy supply of myocardial cells.

To support cardiovascular health, the diet should include fresh fruit and vegetables, wholemeal products, seafood and moderate amounts of wine and chocolate. However, the average German only eats approximately half of the amounts of fruit and vegetables recommended by the German Nutrition Society. Thus, the supply of specific micronutrient combinations is not optimal.

Especially individuals who are at an increased cardiovascular risk or suffer from cardiovascular diseases have a higher than average need for such micronutrients. Moreover, the consumption of chocolate and wine, due to the high fat and alcohol content, can only be recommended within certain limits.

Thus, the supplemental intake of extracted polyphenols from cocoa and grapes is an appropriate alternative. In combinatin with other micronutrients conducive to the health of the heart and vessel, the administration of flavonoids is a useful nutritive dietary support of cardiovascular therapy.
Risk Factors of Cardiovascular Disease

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2. Cocoa Polyphenols (Phytonutrients)
3. Omega-3 Fatty Acids
4. L-Carnitine und Coenzyme Q₁₀
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Folate and vitamin B₆ from diet and supplements in relation to risk of coronary heart disease among women.

Plasma homocysteine and risk for congestive heart failure in adults without prior myocardial infarction.

8 Micronutrient Combinations

Multivitamin supplements are inversely associated with risk of myocardial infarction in men and women
Stockholm Heart Epidemiology Program (SHEEP).
Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study  

Study design, patients and methods

• Case-control study including 15,152 patients with myocardial infarction and 14,820 controls without any symptoms of heart disease or chest pain) from 52 countries in all continents.
• The association between smoking habits, blood pressure, diabetes, abdominal obesity, waist-hip ratio, eating habits, physical exercise, alcohol consumption, apolipoprotein levels, psychosocial factors and cases of myocardial infarction was evaluated.
• Odds Ratios (OR) as well as the population-adjusted risk (PAR) were calculated.

Results

• The following risk factors were significantly associated (p<0.0001 for all risk factors, p=0.03 for alcohol consumption) with acute myocardial infarction:

  • **Smoking** (OR* 2.8 current vs. never)
  • **Increased ApoB-ApoA1 ratio** (OR 3.25 top vs. lowest quintile)
  • **Hypertension** (OR1.91)
  • **Diabetes** (OR 2.37)
  • **Abdominal obesity** (OR 1.12 top vs. lowest tertile and OR 1.62 middle vs. lowest tertile)
  • **Psychosocial factors** (OR 2.67)
  • **Daily consumption of fruits and vegetables** (OR 0.7; by 30% reduced risk)
  • **Moderate alcohol consumption** (OR 0.91; by 9% reduced risk)
  • **Regular physical activity** (OR 0.86; by 14% reduced risk)

• All associations were noted in men and women, old and young, and in all regions of the world.
• Collectively, these 9 risk factors accounted for 90% of the PAR (risk of myocardial infarction) in men and for as much as 94% of the PAR in women.

Conclusion

Abnormal lipids, smoking, hypertension, diabetes, abdominal obesity, psychosocial factors, consumption of fruit, vegetables and alcohol, and regular physical activity account for most of the risk of myocardial infarction worldwide in both sexes and at all ages in all regions. Thus, the approach to prevention and treatment of myocardial infarction can be based on similar principles worldwide. Possibly most premature cases of myocardial infarction could be prevented if these risk factors were given greater attention.

* e.g., OR of 2.8 means a 2.8-fold increased risk (and this is applies to the other OR values correspondingly)
Pycnogenol improves endothelial function in hypertensives

Pycnogenol, French maritime pine bark extract, improves endothelial function of hypertensive patients.

Study design, patients and methods
• In this placebo-controlled double-blind trial 58 hypertensive patients were given 100 mg of pycnogenol (OPC)* or a placebo daily for 12 weeks.

Results
• The treatment with pycnogenol allowed the hypertensive patients to lower the dose of the calcium antagonist nifedipin significantly.
• Moreover, pycnogenol reduced the concentration of the vasoconstrictor endothelin-1 and led to an increase in 6-keto-prostaglandin-F1α levels and thus presumably in the vasodilator prostacyclin.
• In the placebo group a stronger decline in the angiotensin-II concentration was observed than in the pycnogenol group.
• Heart rate, electrolyte and urea levels in the blood did not change significantly in either group.

Conclusion
The intake of pycnogenol allows hypertensive patients to lower the dose of a calcium antagonist and improves endothelial function. As pycnogenol is also able to inhibit thrombocyte aggregation and has antioxidative and antiinflammatory characteristics, the authors recommend pycnogenol administration as supplementary treatment of high blood pressure.

* Pycnogenol: French maritime pine bark extract (Pinus pinaster or Pinus maritima) = OPC: Oligomeric proanthocyanidins
Antioxidants in red wine counteract vascular changes caused by cigarette smoking


Study design, patients and methods
• In this double-blind cross-over trial 16 healthy non-smokers (8 women, 8 men) consumed either:
  - one cigarette
  - one cigarette and one glass of red wine (250 ml)
  - one cigarette and one glass of dealcoholized red wine (250 ml)
• Subsequently the flow-mediated vasodilation (FMD) was determined as parameter for vascular function over a period of 90 minutes.

Results
• Smoking one cigarette impairs vascular function significantly (reduction of FMD) 15, 30 and 60 minutes after inhalation (p<0.001, p<0.001 and p<0.043).
• If the subjects drank one glass of alcohol-containing or dealcoholized red wine at the same time, no FMD change was measured after cigarette smoking.

Conclusion
Thus, the simultaneous consumption of one glass of alcohol-containing or dealcoholized red wine can reduce the detrimental effect of cigarette smoking on vascular function.

The authors assume that the FMD reduction is due to the oxidative stress caused by cigarette smoke. As both types of wine protected the subjects against the effect of cigarette smoke in the same way, not the alcohol but other components of the red wine must be responsible for the beneficial effect.
Resveratrol inhibits platelet aggregation in cardiac patients with aspirin resistance

Resveratrol inhibits aggregation of platelets from high-risk cardiac patients with aspirin resistance.


Study design, patients and methods

• From 31 patients who responded to aspirin therapy (aspirin sensitive) and 19 patients who did not respond to aspirin therapy (aspirin resistant) platelet-rich blood plasma was obtained.

• Based on this blood compartment, platelet aggregation after addition of ADP, collagen or adrenalin with or without resveratrol was measured.

Results

• After ADP addition, platelet aggregation was only slightly influenced by resveratrol.

• The collagen-induced platelet aggregation in the plasma of aspirin resistant subjects could be significantly reduced by resveratrol, whereas resveratrol had little effect on the platelets of aspirin sensitive subjects.

• Comparable results were obtained with adrenalin.

Conclusion

Resveratrol effectively inhibits the collagen- and adrenalin-induced platelet aggregation in aspirin resistant cardiac patients. This mechanism may contribute to the cardio protective effect of resveratrol.

Therefore the authors assume that these patients may benefit from taking resveratrol or related polyphenols.
Dark chocolate improves endothelial and platelet function

Preliminary protocol: In order to assess the effects of dark chocolate on the endothelial function, 5 chronic cigarette smokers underwent the following experimental protocol: Prior to and after the intake of 40 g of dark chocolate and after a 24 hour period of abstinence form polyphenol-rich food, high-resolution ultrasonic images were taken. The ultrasonic examination was repeated 2, 4, 8, and 24 hours after chocolate ingestion.

Main study: Given the positive results of the preliminary study, 20 subjects were randomly divided into two parallel groups. Endothelial function and shear stress dependent platelet function were assessed at baseline after a 24 hour abstinence from food rich in polyphenols and two hours after ingestion of chocolate (either 40 g of dark chocolate or 40 g of white chocolate).

Flow mediated dilatation (FMD) was measured by highly sensitive ultrasonography of the brachial artery.

Results

Dark chocolate significantly improved FMD after two hours compared with baseline (7% vs. 4.4%; p=0.026). The effect of dark chocolate on FMD lasted about eight hours.

Two hours after dark chocolate ingestion platelet aggregation* was reduced from 5% to 3.2% (p=0.03) compared with baseline.

The overall antioxidant status** significantly increased two hours after ingestion of dark chocolate (1.22 vs. 1.25; p=0.03).

No significant effects were seen in the white chocolate group.

Conclusion

Two to eight hours after ingestion, dark chocolate improved arterial blood flow significantly in healthy smokers. It exerts favorable effects on endothelial function and platelet aggregation. These findings are most likely mediated by the antioxidant effect of dark chocolate. White chocolate did not exert such effects.

* demonstrated experimentally through mechanical impact on the platelet suspension (shear stress-induced platelet activation)

** Total antioxidant Status Kit (Randox Laboratories, Crumlin, UK)
Cocoa, blood pressure and cardiovascular mortality

Cocoa intake, blood pressure, and cardiovascular mortality.

Study design, patients and methods
- Prospective cohort study (based on data of the Zutphen Elderly Study)
- 470 elderly men between 65 and 84 years of age, free of cardiovascular diseases at baseline, were followed-up for 15 years. They were divided into three groups based on the cocoa intake: high (>2.3 g cocoa daily), medium (0.4–2.3 g daily) and low (<0.4 g daily) cocoa intake.
- The blood pressure levels were assessed at baseline and after 5 years. During the 15 years of follow-up the deaths were also documented.
- The dietary intake of cocoa was estimated by means of a cross-check dietary history method, especially for cocoa-containing foods. The habitual food consumption was assessed at 5-year intervals (1985–1995) using a food frequency questionnaire.

Results
- One third of the men did not consume cocoa at baseline. The median cocoa intake among users was 2.11 g per day.
- In men with the highest cocoa intake (>2.3 g/d; highest tertile) the mean systolic blood pressure was 3.7 mmHg and the mean diastolic blood pressure was 2.1 mmHg, i.e. both significantly, lower compared to the men with the lowest cocoa intake (lowest tertile, <0.4 g/d; for both systolic and diastolic: p=0.03).
- During follow-up, 314 men died, 152 of cardiovascular diseases.
- Compared with the lowest tertile of cocoa intake, the relative risk for men in the highest tertile to die of cardiovascular diseases was significantly reduced, i.e. by 50% (p=0.004). The all-cause mortality risk was significantly lower by 47% (p<0.001).

Conclusion
In a cohort of elderly men it was demonstrated that high cocoa intake is associated with a decrease in blood pressure.

Also after a 15-year follow-up, cardiovascular and overall mortality could be reduced with higher cocoa consumption.
Effects of low cocoa intake on blood pressure and nitric oxide


Study design, patients and methods
- Randomized, placebo-controlled double-blind study
- Investigators determined the effects of low doses of polyphenol-rich dark chocolate on blood pressure, including 44 adults aged 56–73 years (24 women, 20 men) with untreated upper-range prehypertension (130/85 to 139/85 mmHg) or stage 1 hypertension (140/90 to 160/100 mmHg).
- Parameters such as body weight, plasma lipids, glucose and 8-isoprostane were assessed, also plasma S-nitrosoglutathione* levels, because previous studies had suggested that the increase in the transport form of NO may be associated with vasodilating and blood pressure lowering effects of chocolate.
- The study participants were randomly assigned to receive for 18 weeks either 6.3 g (30 kcal) per day of dark chocolate containing 30 mg of polyphenols (active group) or matching polyphenol-free white chocolate (placebo group).

Results
- From baseline to 18 weeks, dark, polyphenol-rich chocolate intake significantly reduced mean (SD) systolic blood pressure by 2.9% (± 1.6) mmHg and diastolic blood pressure by 1.9% (±1.0) mmHg (p<0.001). Blood pressure levels remained unchanged in the control subjects. Hypertension prevalence declined from 86% to 68%.
- The blood pressure decrease was accompanied by a sustained increase of S-nitrosoglutathione* in the active group (by a mean 0.23 nmol/L; p<0.001). In the placebo group, white chocolate intake caused no changes in blood pressure or plasma biomarkers.
- There were no changes in body weight, plasma levels of lipids, glucose, and 8-isoprostane in both patient groups.

Conclusion
The inclusion of small amounts of polyphenol-rich dark chocolate as part of the diet efficiently reduced blood pressure and improved formation of vasodilative nitric oxide.

* S-nitrosoglutathione: major transport form of bioactive nitric oxide (NO)
Cocoa ingestion improves blood lipids in patients with normal or elevated cholesterol levels

Plasma LDL and HDL cholesterol and oxidized LDL concentrations are altered in normo- and hypercholesterolemic humans after intake of different levels of cocoa powder.


Study design, patients and methods

• Randomized, placebo-controlled double-blind study
• 160 subjects with normal or slightly elevated cholesterol levels ingested for 4 weeks either cocoa powder containing low-polyphenolic compounds (placebo group) or different amounts of cocoa powder (13, 19.5, and 26 g/d) with high-polyphenolic compounds. The cocoa powders were consumed as a beverage after the addition of hot water, twice each day.
• Blood samples were collected at baseline and 4 week after intake of the test beverages for the measurement of plasma total cholesterol, HDL-, LDL- and oxidized LDL-cholesterol concentrations. Additionally the levels of triglycerides and apolipoproteins (Apo) A1, A2 and B were measured.

Results

• In all three subject groups who consumed cocoa beverages with high-polyphenolic compounds for 4 weeks the plasma oxidized LDL concentrations decreased compared with baseline. This effect was shown already after intake of small amounts of high-polyphenolic cocoa (13 g/d).
• When the investigators performed a stratified analysis on 131 subjects who had an elevated LDL cholesterol concentration (≥3.23 mmol/l), plasma LDL cholesterol, oxidized LDL, and apo B concentrations decreased in these subjects, and the plasma HDL cholesterol concentration increased - relative to baseline - with ingestion of low-, middle-, and high-cocoa (all three amounts).

Conclusion

Baba and colleagues conclude from the study results that cocoa polyphenols may contribute to a reduction in LDL cholesterol, an elevation in HDL cholesterol, and the suppression of oxidized LDL.
Impact of chocolate on cardiovascular diseases: a meta-analysis

Chocolate and prevention of cardiovascular disease: a systematic review.

Study design, patients and methods
• Meta-analysis including 136 selected publications (experimental, observational, and clinical studies from MEDLINE research) from 1966 through January 2005, analyzing the relationship between chocolate, cocoa, stearic acid and flavonoids, and the risk of cardiovascular disease (coronary heart disease, stroke).

Results
• Many studies indicate that flavonoid-rich chocolate has a health-promoting effect on the cardiovascular system, since it contributes to:
  - decreasing blood pressure
  - reducing inflammations
  - inhibiting platelet aggregation
  - increasing HDL cholesterol
  - reducing lipid peroxidation (LDL cholesterol oxidation)
  - and improving endothelial function
• The majority of prospective studies on cocoa flavonoids suggest that flavonoid in chocolate may reduce the cardiovascular mortality rate.
• This meta-analysis demonstrates that the consumption of cocoa flavonoids (comparing highest and lowest tertiles) may lower the risk of CHD mortality by 19%.

Conclusion
Therefore the authors conclude that cocoa flavonoids can reduce CHD mortality.
Dark chocolate dilates coronary arteries and reduces platelet aggregation

Dark chocolate improves coronary vasomotion and reduces platelet reactivity.

Study design, patients and methods

• Randomized, placebo-controlled double-blind study
• 22 patients (18 male, 4 female), mean age: 53 years
• The effect of flavonoid-rich dark chocolate on coronary vascular and platelet function was assessed in 22 heart transplant recipients.
• The subjects received 40 g of flavonoid-rich chocolate (70%) or cocoa-free chocolate (placebo control), respectively.
• The coronary vessels of the patients were examined with an angiography catheter and a so-called cold-pressure test (CP-T, immersion of the right hand in ice-cold water) before and 2 hours after ingestion of chocolate.

Results

• Two hours after ingestion of flavonoid-rich chocolate the coronary artery diameter increased significantly (from 2.36 mm to 2.51 mm; p<0.01), whereas it remained unchanged in the control group. Also the endothelium-dependent coronary vasomotion improved significantly after dark chocolate intake (4.5% vs. -4.3% in the control group; p=0.01).
• Furthermore, platelet adhesion* decreased from 4.9% to 3.8% (p=0.04) in the dark chocolate group but remained unchanged in the control group.

Conclusion

Dark chocolate induces coronary vasodilation, improves coronary vascular function, and decreases platelet aggregation 2 hours after consumption. These chocolate effects were paralleled by a significant reduction of oxidative stress and were positively correlated with changes in serum epicatechin** concentration.

* demonstrated experimentally through mechanical impact on the platelet suspension (shear stress-induced platelet activation)
** Epicatechins are included in the class of polyphenols
Opinion of the American Heart Association:
Fish consumption, fish oil, omega-3 fatty acids and cardiovascular disease


Study design, patients and methods

• AHA Science Advisory related to the guidelines established by the Food and Drug Administration (FDA) and the U.S. Environmental Protection Agency.
• Numerous epidemiological studies on the impact of fish and omega-3 fatty acid intake on coronary heart disease, stroke, blood lipids, blood pressure, arrhythmias and thrombosis are discussed.
• Authors also describe the distinction between plant-derived (alpha-linolenic acid) and marine-derived omega-3 fatty acids, e.g. eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).

Results

• Epidemiological and clinical studies demonstrate that omega-3 fatty acids of fish / marine or vegetable origin can reduce the incidence of coronary heart disease.
• Dietary recommendations for omega-3 fatty acids have been made in publications of several countries (e.g. Canada, Sweden, England, Australia, Japan) and by the World Health Organisation and the North Atlantic Treaty Organisation.
• The American Heart Association recommends in its Dietary Guidelines to consume two fish meals per week, with an emphasis on fatty fish (i.e. salmon, herring, and mackerel).
• Moreover, the consumption of vegetable oils containing alpha-linolenic acid (such as soybean and walnut oil) is recommended.
• Patients suffering from coronary heart disease should be encouraged to increase their consumption of EPA and DHA to 1 g per day (which is the dose used in the GISSI-Prevenzione study). As it is difficult to take the required quantity in with the normal diet over a longer period, it is recommended to supplement it with omega-3 fatty acids, and thus reduce the risk of developing coronary heart disease.
• Also for those individuals who do not eat fish, have limited access to a variety of fish, or cannot afford to purchase fish, a fish oil supplement may be considered.
• Supplements of omega-3 fatty acids also could be a component of the medical management of hypertriglyceridemia.

Conclusion

For preventing and treating coronary heart disease, the AHA recommends the consumption of fish or the intake of EPA and DHA supplements.
Dietary supplementation with omega-3 fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial


Study design, patients and methods

• Randomized multicenter trial (130 cardiological departments, 42 rehabilitation centers) with 3.5 years of follow-up.
• 11,324 patients surviving recent (≤3 months) myocardial infarction were randomly assigned to one of four groups to receive these supplementations:
  Group 1:  1 g omega-3 fatty acids
  Group 2:  300 mg vitamin E
  Group 3:  1 g omega-3 fatty acids + 300 mg vitamin E
  Group 4:  no supplementation of micronutrients
• In this study design, investigators evaluated the patients across 2 groups: groups 1 + 3 together were analyzed vs. groups 2 + 4.
• Additionally, an evaluation was made across all four groups. Each experimental group was tested against the control group (no. 4).

Results

• The consumption of omega-3 fatty acids resulted in a significant, i.e. 10%, risk reduction regarding the primary endpoint (i.e. death, survived myocardial infarction, fatal stroke; two-group evaluation) or in a 15% risk reduction (four-group evaluation).
• The total mortality rate was reduced by 14% (two-group evaluation) and 20% (four-group evaluation), the cardiovascular mortality rate was reduced by 17% (two-group evaluation) and 30% (four-group evaluation).

Conclusion

The administration of omega-3 fatty acids (four-group evaluation) resulted in a significant reduction in overall mortality (by 20%), in cardiovascular mortality (by 30%) and in the incidence of sudden cardiac death (by 45%).
Fish and omega-3 fatty acid intake and risk of coronary heart disease in women


Study design, patients and methods
- Cohort study (Nurses Health Study); duration: 16 years
- 84,688 nurses (age range: 34 - 59 years)
- Recording of eating habits based on a food questionnaire
- The study participants had no history of cardiovascular diseases or tumors at baseline.
- Documentation of all survived myocardial infarctions and all deaths due to coronary heart disease (CHD).

Results
- In the course of the study, 484 women died due to CHD, 1,029 women survived a myocardial infarction.
- After adjustment for age, smoking and other cardiovascular risk factors, the investigators found the following association: The higher the consumption of fish or omega-3 fatty acids, the lower the CHD risk (reduction by 21% to 34%).
- The risk of a fatal coronary heart disease was reduced more strongly (by 45%) than the risk of a nonfatal coronary heart disease (by 27%).

Conclusion
Women who consume more fish and omega-3 fatty acids have a lower risk of developing coronary heart disease or of dying due to this disease.
Relation between consumption of fish and omega-3 fatty acids and risk of stroke in women

Intake of fish and omega-3 fatty acids and risk of stroke in women.

Study design, patients and methods
• Cohort study (Nurses Health Study); duration: 14 years
• 79,839 nurses (age range: 34 - 59 years)
• Recording of eating habits based on a food questionnaire
• The study participants had no history of cardiovascular diseases, tumors, diabetes or hypercholesterolemia at baseline.
• Documentation of all ischemic insults (strokes)

Results
• In the course of the study, there were 574 incident strokes (53% ischemic insults = thrombotic or embolic etiology, 31% hemorrhagic insults and 16% insults of unknown etiology).
• After adjustment for age, smoking and other cardiovascular risk factors, the overall stroke risk was all the lower (7-52% reduction, RR: 0.93-0.48), the higher the fish consumption was.
• The risk of suffering a thrombotic insult was 51% lower in women who ate two fish meals per week.
• A high consumption of omega-3 fatty acids was also associated with a reduced risk of strokes (28% reduction, RR:0.82) – primarily of thrombotic insults (33% reduction, RR:0.67).
• The association between consumption of large quantities of fish or omega-3 fatty acids and the reduced risk of strokes of thrombotic etiology was especially strong for women who rarely took aspirin.

Conclusion
The consumption of fish or omega-3 fatty acids reduces the risk of strokes of thrombotic origin.
Early protection against sudden death after myocardial infarction by omega-3 fatty acids (time-course analysis of the results of the GISSI-Prevenzione trial)

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.


Study design, patients and methods

- Subgroup analysis of the GISSI-Prevenzione study including 11,323 patients with recent acute myocardial infarction, focussing on overall mortality and sudden cardiac death; duration: 12 months
- The patients received optimum pharmacological treatment and lifestyle consultation.
- Assignment to 4 groups (see GISSI study) receiving the following daily doses:
  - Group 1: 1 g omega-3 fatty acids
  - Group 2: 300 mg vitamin E
  - Group 3: 1 g omega-3 fatty acids + 300 mg vitamin E
  - Group 4: no supplementation of micronutrients

Results

- The effect of omega-3 fatty acid supplements was already demonstrated after a short time period. After 3 months of treatment, the mortality risk was reduced significantly by 41%, and after 4 months of treatment, the risk of sudden cardiac death was significantly reduced by 53%.
- After 6 to 8 months of treatment with omega-3 fatty acids, study authors also observed a significant reduction in cardiovascular, cardiac or coronary mortality rates.

Conclusion

The effect of low-dose omega-3 fatty acid supplements (1 g per day) on cardiovascular mortality rate and sudden cardiac death confirms the hypothesis of antiarrhythmic effects of omega-3 fatty acids.
Omega-3 fatty acids prevent atrial fibrillation after coronary artery bypass surgery

N-3 fatty acids for the prevention of atrial fibrillation after coronary artery bypass surgery: a randomized, controlled trial.

Study design, patients and methods

- In a group of 160 patients who had undergone coronary artery bypass graft surgery Calò and colleagues determined whether the supplementation of omega-3 fatty acids (polyunsaturated fatty acids, PUFA) prior to and following the surgical procedure could prevent the occurrence of atrial fibrillation.
- Atrial fibrillation is one of the most frequent sequelae of cardiac bypass surgery; it increases the risk of further postoperative complications and prolongs patients’ length of stay in the hospital.
- 79 of the 160 patients (136 males, 24 females, mean age: 66 years) who had to undergo an elective coronary artery bypass graft surgery, randomly received 2 g/day of an omega-3 fatty acid product (eicosapentaenoic : docosahexaenoic acid in relation of 1 : 2). This therapy started at least 5 days prior to the surgical procedure and was continued till the day of discharge from the hospital.
- The residual 81 patients served as controls.
- The primary study endpoint was the electrocardiographically confirmed episode of atrial fibrillation, either lasting at least 5 minutes or leading to angina or hemodynamic compromise requiring intervention.

Results

- The clinical and surgical characteristics of the patients in the two groups were similar, and there was no significant difference either in the postoperative mortality (1.3% vs. 2.5% in PUFA-treated vs. control patients) or in the incidence of nonfatal postoperative complications between patients with or without PUFA supplementation.
- Postoperative atrial fibrillation developed in only 15.2% versus 33.3% (12 vs. 27 patients) in the PUFA group vs. controls (p=0.013). Also, after bypass graft surgery the time of hospitalization of PUFA patients was significantly shorter than of controls (7 days vs. 8 days, p=0.017).
- In multivariate analysis the intake of PUFAs (with an OR of 0.32), beside age, was noted to be the only significant independent predictor of postoperative atrial fibrillation.

Conclusion

Omega-3 polyunsaturated fatty acid supplementation in patients undergoing isolated coronary artery bypass graft surgery significantly reduces the occurrence of postoperative atrial fibrillation (by 54%), with this effect being similar to that obtained with beta-blockers, sotalol, and amiodarone. Moreover, patients in the PUFA group were hospitalized for significantly fewer days than those in the control group.
Preventing sudden death with omega-3 fatty acids

Preventing sudden death with n-3 (omega-3) fatty acids and defibrillators.

Study design, patients and methods
• Based on the antiarrhythmic effects of omega-3 fatty acids, the hypothesis was to be examined according to which these nutrients, if administered on a regular basis, could reduce the mortality rate in the population.
• As previous studies have shown, various interventions are able to reduce the incidence of sudden cardiac death: using omega-3 fatty acids, widely distributing automated external defibrillators (AED), and implanting cardioverter defibrillators (ICD) in appropriate candidates. As, however, the target groups for these measures differ considerably in many ways, it may be difficult to compare their effectiveness in a study.
• Thus, the scientists used a mathematical model in order to simulate the effects of various strategies on mortality. Approximately 95% of a hypothetical population between 30 and 84 years had a healthy heart, in the remaining subjects a heart disease (predominantly coronary heart disease) had already been diagnosed.

Results
• During the observational period of 3 years, the mortality rate in the experimental group could be reduced by around 6.4% through raising the omega-3 fatty acid levels, the investigators estimated. Distributing automated external defibrillators or implanting ICDs was expected to lower total mortality by 0.8% and 3.3%, respectively, according to this model.

Conclusion
In order to reduce rates of sudden death in a representative population, it would, mathematically, be about eight times more effective to raise omega-3 fatty acid levels than to distribute external defibrillators, and two times more effective than implanting internal cardioverter / defibrillators in high-risk patients. Three fourths of the reduction in total mortality due to omega-3 fatty acid augmentation would accrue from raising omega-3 fatty acid levels in the healthy population.
Low-dose docosahexaenoic acid lowers diastolic blood pressure in middle-aged men and women

Low-dose docosahexaenoic acid lowers diastolic blood pressure in middle-aged men and women.

Study design, patients and methods
• In this double-blind, randomized placebo-controlled crossover study, 38 healthy subjects between 45 and 65 years received 0.7 g docosahexaenoic acid (DHA*) or placebo (olive oil) for 3 months. After a wash-out phase of 4 months, the groups were exchanged and the treatment was continued for another 3 months.
• Both at baseline and at the end of each study phase various relevant serum parameters, vascular function as well as blood pressure and heart rate were measured.

Results
• Supplementing of DHA markedly raised the DHA proportion of the total erythrocyte lipids by a mean of 58%.
• Neither the arterial compliance nor the endothelium-derived (glyceryl trinitrate) or endothelium-independent (salbutamol) pharmacological responses were influenced by the intake of DHA, and plasma levels of CRP, soluble thrombomodulin, E-selectin and von-Willebrand factor antigen or the urinary microalbumin or isoprostane excretion did not differ between DHA and placebo group.
• The diastolic blood pressure was, however, lowered significantly through DHA supplementation by an average of 3.3 mmHg (p=0.01).

Conclusion
The moderate increase in the daily intake of DHA to about 700 mg for 3 months significantly lowers diastolic blood pressure in healthy middle-aged individuals, which in turn could potentially reduce the risk of cardiovascular events.

* Docosahexaenoic acid (DHA): long-chain, polyunsaturated fatty acid, omega-3 fatty acid
High fish consumption protects against arrhythmia

Long-term fish consumption is associated with protection against arrhythmia in healthy persons in a Mediterranean region – the ATTICA study.


Study design, patients and methods

• A diet rich in fish has, according to existing research, a favorable impact on cardiac health. For this the polyunsaturated omega-3 fatty acids appear to be responsible primarily, which stabilize the heart muscle and protect it against arrhythmias.
• In this cross-sectional study the Greek authors compared the fish consumption with the heart rate corrected QT duration (QTc) which is considered a reliable measure to determine the arrhythmia risk of an individual.
• More than 3,000 subjects provided information on their diet using validated food-frequency questionnaires, on their socio-demographic situation and various lifestyle factors.
• Additionally, an ECG was performed and blood pressure measured in all participants. Subjects with already existing cardiovascular diseases were excluded from the study.

Results

• According to subjects’ self reports, the majority of them (88% of men, 91% of women) were eating at least one 150-g meal of fish per week.
• The QTc duration in those who consumed more than 300 g fish per week was, on an average, 13.6% shorter than in those who did not eat any fish.
• In this group abnormal QTc values (>0.45 s) were by about 29% less likely to occur than in the group without any fish consumption.
• Even if the researchers adjusted values for other relevant potential confounders, the beneficial impact of fish-enriched diet on the risk of arrhythmias still remained.

Conclusion

Individuals who eat a fish-enriched diet are likely to show a shorter QTc duration in the ECG findings and are thus less at risk of arrhythmias than those who eat little or no fish at all. These current results support the favorable effect of omega-3 fatty acids on cardiac health as already demonstrated in other studies.
Carnitine and its role in cardiovascular disease

Study design, patients and methods
• Review summarizing 39 animal models, epidemiological and clinical studies about the effect of carnitine on cardiovascular disease.

Results
• Carnitine is a natural endogenic substance performing a variety of physiological functions. Thus, for instance, it plays a significant role in the transport of the fatty acids required for energy supply. As the human heart uses fatty acids as an important source of energy, it is obvious that carnitine deficiency may lead to cardiac dysfunction.
• Additionally, carnitine accelerates the elimination of waste products and thus reduces the intracellular concentration of cytotoxic substances, such as acyl esters or free radicals.
• Carnitine supplementation has a beneficial effect on the treatment of patients who are deficient in carnitine (e.g. patients with coronary heart disease, myocardial hypertrophy, diabetes).
• Clinical studies and animal models show that carnitine can be used very effectively in the treatment of cardiovascular diseases (such as coronary heart disease, peripheral arterial disease, arrhythmias, heart failure, and hyperlipidemia). Thus, for instance, in patients suffering from heart failure who received carnitine exercise tolerance and left ventricular ejection fraction of the heart could be improved.

Conclusion
L-carnitine plays an important role in cardiac energy supply and cardiac metabolism and thus contributes to better functional ability of both the healthy and the diseased heart.
Dose-related decrease of serum coenzyme Q₁₀ by treatment with statins


Study design, patients and methods
- Randomized double-blind study, duration: 18 months
- 45 patients (men and women) with high cholesterol levels (250 - 500 mg/dl); age range: 30 - 75 years
- 7 week run-in phase during which subjects were given dietary recommendations and placebo
- Assignment of subjects to one of 2 groups and 18-month treatment with a rising daily dose of a statin:
  - Group 1: lovastatin 20 mg, 40 mg, 80 mg
  - Group 2: pravastatin 10 mg, 20 mg, 40 mg

Results
- Statins, such as lovastatin and pravastatin, inhibit the HMG-CoA reductase enzyme and thus the new synthesis of cholesterol and coenzyme Q₁₀ (also called ubiquinone).
- Coenzyme Q₁₀ is packed in LDL and VLDL particles and thus, as an antioxidant, presumably prevents their oxidation and, as a result, the risk of atherosclerosis.
- After 6 weeks already, both pravastatin and lovastatin led to a significant reduction in LDL and VLDL cholesterol.
- In this way, the two statins significantly lowered the serum coenzyme Q₁₀ levels by as much as 19.7% (p<0.01; pravastatin) and 28.8% (p<0.001; lovastatin) after 18 months of treatment.

Conclusion
It was shown in a pilot study that statin treatment can impair cardiac function and that this condition can be improved when patients are given coenzyme Q₁₀. To make sure that the beneficial cholesterol-reducing effect of statins is not weakened by a coenzyme Q₁₀ reduction, coenzyme Q₁₀ supplementation should be provided for patients taking statins for a longer period.
Atorvastatin decreases the coenzyme Q\(_{10}\) level of patients at risk of cardiovascular disease and stroke


Study design, patients and methods

- Prospective single-blind study to investigate the effect of short-term atorvastatin administration (80 mg/day for 14 – 30 days) on the blood coenzyme Q\(_{10}\) level.
- 34 hypercholesterolemic patients (>45 years) of a hospital stroke unit who met the criteria of the National Cholesterol Education Program "Adult Treatment Panel III" for statin treatment, i.e. they had:
  a) coronary heart disease (CHD) or similar symptoms (e.g. peripheral arterial disease, symptomatocarotid ateriosclerosis, diabetes mellitus)
  b) several CHD risk factors and an LDL cholesterol of 130 mg/dl
  c) no or only one risk factor and an LDL cholesterol of >160 mg/dl

Results

- The average blood coenzyme Q\(_{10}\) level at the start of the study was 1.26±0.47 µg/ml and after a 30-day atorvastatin therapy it dropped by 52% to 0.62 ± 0.39 µg/ml (p<0.001).
- A significant decline in the blood coenzyme Q\(_{10}\) level by 49% to 0.67 µg/ml was stated after 14 days already (p<0.001).

Conclusion

Statins are used routinely in the treatment of hypercholesterolemia and coronary heart disease as well as for stroke prevention.

In this study, the short-term administration of atorvastatin already led to a significant reduction in the coenzyme Q\(_{10}\) level. The inhibition of the cholesterol synthesis by statins is associated with a reduction of the coenzyme Q\(_{10}\) synthesis.

Presumably, low coenzyme Q\(_{10}\) values are responsible for the most frequent adverse events of statin treatment affecting the skeletal muscles (e.g. myalgia, myoglobinuria, and difficulties under physical stress).
Antioxidant supplementation enhances antioxidant capacity and reduces oxidative damage following ischaemic stroke


**Study design, patients and methods**

- In this study, 48 stroke patients within 12 hours of symptom onset were randomly administered either 727 mg vitamin E (alpha-tocopherol) and 500 mg vitamin C, or no supplementation. This intervention was continued for 14 days.

**Results**

- Antioxidant supplementation significantly improved antioxidant concentrations (p<0.005) and total antioxidative capacity (p<0.003).
- Furthermore, authors observed a significant reduction in oxidative stress in the treatment group.
- This was demonstrated by the significant reduction of malondialdehyde level and thus lipid peroxidation (p<0.002).
- The inflammation marker CRP was also reduced significantly (p<0.02).

**Conclusion**

Supplementation with antioxidant vitamins within 12 hours of onset of acute ischemic stroke significantly increased antioxidant capacity, reduced oxidative stress and may have an antiinflammatory effect.
Correlation between vitamin concentrations after ischemic stroke and inflammation markers and neurological deficits

Plasma levels of lipophilic antioxidant vitamins in acute ischemic stroke patients: correlation to inflammation markers and neurological deficits.

Study design, patients and methods
• The authors of the study measured the concentrations of fat-soluble antioxidant vitamins and phytonutrients (retinol, alpha- and gamma-tocopherol as well as lycopene, alpha-carotene and beta-carotene) and inflammation markers, such as CRP, in 68 patients with acute ischemic stroke within 48 hours after stroke onset, in comparison with the values of 41 normal controls.
• The aim was to study the correlation between these measured values and the neurological deficits of the patients.

Results
• In this study, stroke patients showed significantly lower alpha- and beta-carotene levels than normal subjects.
• Researchers found an inverse correlation between low carotene levels and the increased inflammation marker “high-sensitivity C-reactive protein” (hs-CRP, p<0.01) and the occurrence of neurological deficits (p<0.05).
• However, the magnitude of inverse correlation between the values for alpha- and beta-carotene combined and the neurological deficits decreased after adjustment of hs-CRP (p=0.08).

Conclusion
Patients with acute ischemic stroke seem to have lower alpha- and beta-carotene levels than normal subjects, and a negative association can be detected between these low carotene levels and the inflammation marker hs-CRP.

As the hs-CRP values affect the correlation between carotenes and neurological deficits, hs-CRP concentrations should be taken into account when using carotene levels as predictors of neurological deficits after ischemic stroke.
Vitamin C and risk of coronary heart disease in women

Study design, patients and methods
- Prospective cohort study (Nurses Health Study); duration: 16 years
- 85,118 nurses (age range: 30 - 55 years)
- Recording of eating habits based on a food questionnaire
- Women who had existing cardiovascular diseases or tumors were excluded from the study.
- Documentation of all survived myocardial infarctions and all deaths due to coronary heart disease (CHD).

Results
- Between 1980 and 1996, 1,356 incident cases of CHD were recorded.
- After statistical adjustment for coronary risk factors (such as age, smoking, etc.), it could be demonstrated that a high vitamin C consumption (≥ 360 mg/day) was associated with a reduced risk of myocardial infarction (reduction by 27%).
- The intake of vitamin C alone with the diet, without multivitamin supplementation, resulted in a weak and not significant CHD risk reduction.
- In multivariate models it was found that in women with daily vitamin C supplementation, the vitamin C intake was associated with a 28% reduction in the CHD risk compared with women who did not take any vitamin C supplement.

Conclusion
Individuals taking vitamin C supplements appear to be at lower risk of CHD development.
Effect of six years of combined vitamin C and E supplementation on atherosclerotic progression (ASAP study)

Six-year effect of combined vitamin C and E supplementation on atherosclerotic progression: the Antioxidant Supplementation in Atherosclerosis Prevention (ASAP) study.

Study design, patients and methods
• Placebo-controlled, double-blind study; duration: 6 years
• 520 subjects (256 men and 264 postmenopausal women; smokers and non-smokers, with serum cholesterol levels of ≥193 mg/dl)
• Age range: 45 - 69 years
• Ultrasonographically assessed atherosclerotic vascular alterations
• Vitamin supplementation: 136 I.U. Vitamin E and 250 mg Vitamin C, each twice daily with a meal.

Results
• Study participants taking vitamins demonstrate in the 6-year course of the study a reduction in the slope of mean CCA-IMT* (reduction in slope increase 33% for men, 14% for women).
• In both sexes combined, the average annual increase in mean internal vascular wall thickness was 0.014 mm in the unsupplemented and 0.010 mm in the supplemented group, which amounts to a treatment effect of 25%.
• The effect of vitamin intake was largest in subjects who had low baseline plasma vitamin C levels or had already developed plaques in the common carotid artery.

Conclusion
The supplementation with a combination of vitamins E and C significantly slowed down the atherosclerotic progression in hypercholesterolemic patients.

* CCA: common carotid artery; IMT: intima-media thickness
Vitamin B<sub>1</sub> deficiency and heart failure

The prevalence of thiamin deficiency in hospitalized patients with congestive heart failure.


Study design, patients and methods

• The water-soluble vitamin B<sub>1</sub> (thiamin) functions as a coenzyme in oxidative metabolic processes, such as the production of cellular adenosine tri-phosphate. As mammals, and humans, cannot biosynthesize thiamin or store it to any appreciable extent, they are dependent on continual ingestion through the diet. Thiamin deficiency, among other disorders, leads to neurological dysfunctions, and also to sodium and water retention, peripheral vasodilation and myocardial failure. Therefore, thiamin deficiency would be expected to worsen symptoms in the setting of established congestive heart failure (CHF).

• The objective of Canadian researchers was to verify this hypothesis in a prospective, randomized cross-sectional study including 100 hospitalized patients with congestive heart failure, and 50 normal controls. Beside fasting erythrocyte thiamin pyrophosphate concentrations, also thiamin intake (through diet and/or supplements), urine thiamin loss and other relevant clinical parameters were measured.

Results

• Thiamin deficiency was more prevalent in CHF patients compared to healthy control subjects (33% vs. 12%; p=0.007).

• The degree of disease severity (left ventricle function according to NYHA classification) apparently influenced the risk of thiamin deficiency (NYHA grade III/IV: 40% vs. NYHA grade I/II: 25%, n.s.). This difference was accentuated when supplement users were excluded.

• According to univariate analysis of determinants of thiamin deficiency, patients with preadmission spironolactone use – a possible indication of the severity of heart failure – and those who were non-users of thiamin-containing supplements, were most likely to show thiamin deficiency (p<0.05).

Conclusion

Deficiency of vitamin B<sub>1</sub> is more prevalent in patients with congestive heart failure than in normal controls, and supplementation of thiamin-containing multivitamin products may be protective against thiamin deficiency.

Thus, the daily thiamin supplementation may reduce the risk of developing a deficiency in this patient population.
Folic acid therapy reduces homocysteine levels in hemodialysis patients


Study design, patients and methods

• Alvares Delfino and colleagues included in their study 46 patients with renal failure who had to undergo hemodialysis for at least 4 months 3 times per week.
• They were randomly assigned to receive for 6 months 10 mg of folic acid (26 patients) or placebo (20 patients) after each dialysis.
• Before and after completion of the 6-month therapy homocysteine levels and – as a marker of oxidative stress – total plasma antioxidant capacity, as well as hydroperoxide levels were measured and compared.

Results

• Compared to baseline values, the treatment with folic acid significantly reduced homocysteine levels. Simultaneously, antioxidant capacity was increased, while the hydroperoxide levels remained unchanged.
• In the patients of the placebo group there were no significant changes in the parameters assessed.

Conclusion

Folic acid therapy on a regular basis may effectively lower plasma homocysteine levels in hemodialysis patients already within a period of 6 months.

Thus, such an intervention may decrease the risk of cardiovascular events and consequently cardiovascular mortality in patients with chronic kidney disease.
Folic acid supplementation in the prevention of arteriosclerosis

Effect of short-term folic acid supplementation on insulin sensitivity and inflammatory markers in overweight subjects.

Study design, patients and methods

• Inflammation plays a pivotal role in the atherosclerotic process. As high serum homocysteine levels increase the concentrations of certain cytokines and chemokines as well as insulin resistance, they contribute to the risk of developing cardiovascular disease. Now an Italian research group examined whether and to what extent these atherosclerosis markers may be beneficially influenced by folic acid supplementation (via reduction of homocysteine levels).
• The participants of this prospective placebo-controlled study were 60 healthy volunteers with normal glucose tolerance and BMI between 25 and 29 kg/m2. Among them, one half (n=30) received 2.5 mg/day of folic acid, the other half (n=30) received placebo, for 12 weeks. Potential effects of this supplementation were evaluated based on extensive laboratory tests.

Results

• With the 3-month supplementation of folic acid, serum folate levels were significantly increased, while homocysteine levels were decreased. Simultaneously, the serum levels of C-reactive protein (CRP), IL-8 and MCP-1* dropped significantly, and the alterations of these inflammation markers were associated with a rise in folate levels. Moreover, the fasting insulin level and the HOMA** index – a measure of insulin resistance – improved. Here again investigators could demonstrate a close relationship between alterations of MCP-1 concentrations and HOMA index.

Conclusion

In healthy overweight adults already a short-term folic acid supplementation reduces the circulating levels of homocysteine and of other inflammatory mediators that contribute to atherogenesis. The simultaneous drop in fasting insulin level and HOMA index, independently of weight change, thus suggests a potential therapeutic effect of folic acid on glucose regulation.

The supplementation of folic acid therefore could be an important approach to the prevention of cardiovascular disease.

* MCP-1: macrophage chemoattractant protein-1
** HOMA: homeostasis model assessment
Improvement in stroke mortality by folic acid enrichment


Study design, patients and methods

• In a recent, large population-based cohort study, North American researchers evaluated whether the consistent folic acid fortification of enriched grain products – as it has been implemented in the United States and Canada since 1998 – beneficially influences stroke mortality.
• Q. Yang and colleagues compared the number of stroke-related deaths in the United States and Canada with those in England and Wales, where folic acid fortification is not required. The time period evaluated includes the years 1990 to 2002.

Results

While the rate of decline did not change significantly in England and Wales, in North America the decline in mortality accelerated after the implementation of the folic acid fortification program in men and women and in all age groups examined. Thus, stroke-related mortality in the United States was annually reduced by 0.3% before 1998, but by 2.9% per year after 1998. In Canada the corresponding annual rates were 1.0% before vs. 5.4% after implementation of folic acid fortification. According to the authors, other risk factors or changes in overall mortality did not have any effect on this development. Data available for the United States demonstrated that after the implementation of folic acid enrichment and parallel to the decline in stroke mortality, folate levels as well as serum homocysteine levels decreased in people of ≥40 years of age.

Conclusion

The consistently higher intake of folic acid is an appropriate means to reduce the stroke-related number of deaths on a population-wide basis. An increased serum homocysteine concentration, an independent risk factor for cardiovascular diseases including stroke, can be effectively lowered by folic acid intake.
Effect of homocysteine-lowering therapy with folic acid, vitamin B₁₂ and vitamin B₆ on restenosis rate after PTCA: the Swiss Heart study

Effect of homocysteine-lowering therapy with folic acid, vitamin B₁₂, and vitamin B₆ on clinical outcome after percutaneous coronary intervention: The Swiss Heart study: a randomized controlled trial.

Study design, patients and methods
• Randomized, double-blind placebo-controlled trial involving 553 patients after successful angioplasty of at least one significant coronary stenosis (= elimination of a vascular occlusion and enlargement of the vessel lumen; also called PTCA, percutaneous transluminal coronary angioplasty)
• Combination of folic acid (1 mg/d), vitamin B₁₂ (400 µg/d), and vitamin B₆ (10 mg/d), or placebo, for 6 months
• Follow-up period: 11 months
• A composite endpoint of major adverse events was measured (major adverse events defined as death, nonfatal myocardial infarction, and need for repeat revascularization).

Results
• After almost 1 year, the risk in the composite endpoint was 32% lower due to folic-acid, vitamins B₆ and B₁₂ intake.
• A non-significant trend was seen toward fewer deaths, nonfatal myocardial infarctions and repeat revascularizations of the stenoses (reduction of 7.4%), compared to the placebo group (15.4% vs. 22.8%), primarily due to a reduced rate of target lesion revascularization.
• Thus a recurrent vessel occlusion was only seen in 9.9% of the supplementation group, but in 16% of the patients in the placebo group.

Conclusion
The intake of folic acid, vitamins B₆ and B₁₂ not only reduces high homocysteine levels, but also significantly decreases the rate of restenosis after percutaneous transluminal coronary angioplasty (PTCA).
Folic acid and vitamin B6 from diet and supplements in relation to risk of coronary heart disease among women

Folate and vitamin B6 from diet and supplements in relation to risk of coronary heart disease among women.

Study design, patients and methods
• Prospective cohort study (Nurses Health Study); duration: 14 years
• 80,082 nurses (age range: 30 - 55 years)
• The study participants had no history of cardiovascular diseases, tumors, diabetes or hypercholesterolemia at baseline.
• Recording of eating habits and consumption of supplements based on a food questionnaire
• Evaluation of the relationship between risk of coronary heart disease (CHD) and the consumption of folic acid and vitamin B6.

Results
• During the study period, 658 incident cases of nonfatal myocardial infarctions and 281 cases of fatal CHD were recorded.
• After adjustment for cardiovascular risk factors (hypertension, etc.) and smoking habits, in women who consumed more than 696 µg of folic acid per day researchers observed a 31% reduction in CHD risk compared to women who consumed less than 158 µg of folic acid per day.
• Women who consumed more than 4.6 mg of vitamin B6 per day, showed a reduced risk of CHD (33%) compared to women who consumed less than 1.1 mg of vitamin B6 per day.
• In women with a high consumption of folic acid and vitamin B6 combined, the reduction of CHD risk was 45%.
• Women who regularly used multivitamins had a reduction in CHD risk of 24%.

Conclusion
The study results suggest that the intake of folic acid and vitamin B6 above the currently recommended dietary allowance may be important in the primary prevention of CHD among women.
Homocysteine levels and risk of congestive heart failure in adults without prior myocardial infarction


Study design, patients and methods
• Prospective cohort study; duration: 8 years
• 2,491 adults (thereof 1,547 women, average age: 72 years)
• All subjects had participated in the Framingham Heart Study in the period from 1979-82 and 1986-90 and, at the beginning of the study, did not show any signs of heart failure or a prior myocardial infarction.

Results
• In the study period, 156 participants suffered a heart failure (88 of them women).
• After adjusting the results for other risk factors, it was found that an increased plasma homocysteine level (>11.1 µmol/l) was associated with a 1.93-fold higher risk of heart failure in women.
• Moreover, for men a plasma homocysteine level of more than 11.8 µmol/l was associated with a 1.84-fold higher risk of heart failure.
• The association between an increased homocysteine level and heart failure was more evenly distributed in women than in men.
• If the analysis was limited to subjects who had not had any coronary heart disease at the beginning of the study, the same correlation between plasma homocysteine level and heart failure risk was found.

Conclusion
An elevated plasma homocysteine level is an independent risk factor which increases the probability of developing heart failure at a later time.
Multivitamin supplements are inversely associated with risk of myocardial infarction in men and women: Stockholm Heart Epidemiology Program (SHEEP)


Study design, patients and methods
- Case-control study (2,981 patients, age range: 45 - 70 years)
- Documentation of eating habits and intake of supplements based on a questionnaire
- Comparison between 1,296 patients (910 men, 386 women) who had survived a myocardial infarction, and 1,685 healthy control subjects (1,143 men, 542 women).
- Multivitamin supplements were taken by 27% of the men and 42% of the women in the myocardial infarction group, and by 35% of the men and 57% of the women in the control group.
- 80% of these supplements were multivitamin products. 10% of the users took separate vitamin C and 2% took separate vitamin E supplements.

Results
- After statistical adjustment for influencing factors such as age, smoking habits, consumption of fruit and vegetables as well as dietary fiber, the myocardial infarction risk of men and women who took supplements was lower by 21% and 34%, respectively.
- Especially smoking women benefited from taking supplements.

Conclusion
The results of this study show that taking micronutrients contributes to primary prevention of cardiovascular disease.