

Citation:

Rasmussen BM, Vessby B, Uusitupa M, Berglund L, Pedersen E, Riccardi G, Rivellese AA, Tapsell L, Hermansen K. Effects of dietary saturated, monounsaturated, and n-3 fatty acids on blood pressure in healthy subjects, *Am J Clin Nutr*. 2006 83: 221-226.

PubMed ID: [16469978](#)

Study Design:

Randomized controlled trial; parallel, multi-center study

Class:

A - [Click here](#) for explanation of classification scheme.

Research Design and Implementation Rating:

 NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

- The purpose was to investigate whether dietary monounsaturated fatty acids (MUFA), compared with saturated fatty acids (SFA) affects blood pressure (BP) in healthy adults
- A secondary purpose was to investigate whether the addition of long-chain n-3 fatty acids had an effect on BP.

Inclusion Criteria:

- Healthy adults
- Normotensive
- Normal or moderately increased body weight (BMI: 22 to 32)
- Impaired glucose tolerance was acceptable.

Exclusion Criteria:

- Diabetes
- Specific eating habits, due to cultural or religious beliefs
- High habitual physical exercise
- High alcohol intake (binge drinking or a regular intake of over 40g alcohol per day)
- Hepatic, cardiac, thyroid or disabling disease
- Body weight change during past three months of over four kg
- Subjects taking acetyl salicylic acid, thiazide diuretics, beta blockers, lipid-lowering drgs or corticosteroids.

Description of Study Protocol:**Recruitment**

Not discussed.

Design

- Three-month controlled parallel, multicenter study with a two-week run-in period, followed by randomization to one of two groups: MUFA or SFA
- Within each of the two groups, there was further randomization to receiving supplementary n-3 fatty acids or a placebo of olive oil.

Blinding Used

Subjects were blinded to n-3 fatty acid or olive oil supplementation.

Intervention (if applicable)

- Isoenergetic diets with the same amount of macronutrients were consumed for three months
- 37% of kcalories from fat was used for both the high-MUFA and the high-SFA diets
- The MUFA diet consisted of 8% of kcalories from SFA, 23% from MUFA and 6% from PUFA
- The SFA diet consisted of 17% SFA, 14% from MUFA and 6% from PUFA
- Randomized subgroups from the MUFA group and from the SFA group received additional fish oil capsules with 3.6g n-3 fatty acids per day (2.4g as EPA and DHA)
- Trained dietitians instructed all subject on preparation of their diets and met with subjects at least every other week until the end of the study
- Edible fats were supplied to use as spreads, for cooking and in dressings that contained negligible amounts of trans fatty acids, n-3 fatty acids or olive oil.

Statistical Analysis

Data was analyzed as an intention to treat study including all randomized subjects with at least one measurement during treatment. A statistical model that is not described was used with treatment categories of SFA or MUFA with or without n-3 fatty acids and their interaction analyzed as factors. Center, age, sex, and baseline value of the outcome variable were covariates. A post hoc subgroup analysis of total fat intake above or below 37% of kcalories was conducted.

Student's unpaired t tests were used to determine differences between groups.

Data Collection Summary:

Timing of Measurements

- BP was measured at baseline and at the end of the study (three months)
- Weight was measured at each visit (every two weeks).

Dependent Variables

- *Variable One:* Diastolic BP
- *Variable Two:* Systolic BP
- Both DBP and SBP were measured to the nearest five mm Hg with a sphygmomanometer in a sitting position, after 10 minutes of rest
- Measurements were done three times at two-minute intervals and a mean value was used.

Independent Variables

- *SFA diet:* 37% of energy as fat with high proportion of SFAs
- *MUFA diet:* 37% of energy as fat with high proportion of MUFAs
- Fish oil supplement (3.6g n-3 fatty acids per day providing 2.4g EPA and DHA).

Control Variables

Placebo (olive oil) supplement.

Description of Actual Data Sample:

Initial N

162; 95 men and 67 women.

Attrition (final N)

162 because of intent to treat analysis, however three dropped out.

Age

- 30 to 65 years
 - *SFA/placebo group (N=42): 49.3±7.1 (mean±SD)*
 - *SFA/n-3FA group (N=41): 48.5±8.0*
 - *MUFA/placebo group (N=40): 47.0±8.8*
 - *MUFA/n-3 FA group (N=39): 49.5±7.3.*

Ethnicity

Not described.

Other Relevant Demographics

None given.

Anthropometrics

- BMI was not different between groups, nor did it change during the course of the study
- BMI
 - *SFA/placebo group: 26.3±2.7*
 - *SFA/n-3 group: 26.9±3.0*
 - *MUFA/placebo group: 26.1±3.2*
 - *MUFA/n-3 group: 26.5±3.1.*

Location

Five centers: Denmark, Sweden, Finland, Italy and Australia.

Summary of Results:

There were no differences between the groups for SBP or DBP at baseline.

Effect of Three-Month Dietary Intervention and n-3 Fatty Acids on DBP and SBP

	SFA Baseline	SFA Change	P-Value	MUFA Baseline	MUFA Change	P-Value	Mean Difference; 95% CI	P-Value
<i>DBP (mm Hg) Placebo</i>								
<37% of energy	76.2±6.8	1.9±8.2	0.07	78.3±11.8	-4.8±8.5	0.02	6.4; 2.3, 10.5	0.0023
>37% of energy	78.2±8.4	-2.7±5.3	0.01	77.3±8.1	-2.1±7.8	0.18	-1.7; -5.6, 2.2	0.3973
<i>DBP n-3 fatty acids</i>								
<37% of energy	74.4±8.7	-1.0±6.4	-1.3	74.2±9.0	-2.3±6.3	0.09	1.7; -2.3, 5.7	0.4107
>37% of energy	79.7±8.6	-1.3±6	-1.6	74.9±9.6	-3.4±5.1	0.02	1.8; -2.4, 5.9	0.3940

<i>SBP Placebo</i>								
<37% of energy	122.4±10.3	3.5±11.6	0.16	125.8±16.8	-4.8±8.2	0.15	6.6; 0.3, 12.9	0.0408
>37% of energy	120.8±12.8	-3.2±5.7	0.0524	120.7±16.4	-2.4±11.6	0.26	-1.9; -7.9, 4.1	0.5286
<i>SBP n-3 fatty acids</i>								
<37% of energy	121.1±11.1	-2.1±13.2	0.29	125.0±10.1	-2.3±10.9	0.29	-0.1; -6.3,6.0	0.9691
>37% of energy	124.1±11.7	-1.4±7.1	0.56	119.5±15.4	-3.2±11.9	0.28	1.3; -5.0, 7.7	-0.6802

- Values are mean±SD; far right two columns are differences in treatment effects of SFA vs. MUFA
- There was a significant drop from baseline in SBP for the MUFA treated group (-2.2%; P=0.009) and for DBP (-3.8%; P=0.0001) without significant changes for the SFA diet group
- The MUFA diet caused lower DBP than the SFA diet (P=0.0475)
- The table above shows the changes from baseline with the added covariate of less than or more than 37% of total kcalories as fat
- When total fat was under 37%, the MUFA diet reduced SBP and the DBP
- These differences disappeared when fat intake was above 37% of kcalories
- There was no effect of added n-3 fatty acids.

Author Conclusion:

- Decreasing SFA and increasing MUFA decreased diastolic BP
- The beneficial effect on BP from type of fat was negated by consumption of a high total fat intake (>37% of kcalories from fat)
- The addition of n-3 fatty acids had no effect on BP.

Reviewer Comments:

- *Double-blinding was not used*
- *Weight, exercise and smoking habits were kept stable for the duration of the study*
- *Compliance was checked by diet records and serum phospholipid fatty acid composition*
- *There was a slightly higher dietary fiber intake and lower cholesterol intake by the MUFA group*
- *There was no difference in calculated dietary intakes of calcium, sodium, potassium and alcohol between the groups.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1. Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)
2. Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?

Yes

Yes

3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	Was the research question clearly stated?	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	???
2.	Was the selection of study subjects/patients free from bias?	???
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	No
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	Were study groups comparable?	No
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	No
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	No
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	Was method of handling withdrawals described?	Yes
4.1.	Were follow-up methods described and the same for all groups?	No
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	???

4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	Was blinding used to prevent introduction of bias?	???
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	???
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	???
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	???
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	Were outcomes clearly defined and the measurements valid and reliable?	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	Was the statistical analysis appropriate for the study design and type of outcome indicators?	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes

8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	Are conclusions supported by results with biases and limitations taken into consideration?	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	Is bias due to study's funding or sponsorship unlikely?	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes

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