
Declining rates of CHD mortality observed in the US could be due to declining incidence of CHD, declining severity of CHD, and/or improving management of CHD. We examined trends in severity of hospitalized MI to characterize its potential contribution to this decline. Data from the community surveillance component of the ARIC Study were examined for the period 1987 through 1994 for all hospitalizations that met criteria for definite or probable MI (N = 4,903). Hemodynamic, electrocardiographic and enzymatic indicators of severity of MI and diagnostic categories were examined. Temporal trends in these severity indicators were tested with adjustment for age, sex, race, and community (and use of thrombolytics for peak CK). No significant temporal change in the proportion having SBP < 100 mm Hg or an abnormal pulse was noted. The proportion with ST elevation on the initial ECG increased 10% per year (p < 0.001), whereas, the proportion that developed a new Q-wave during the hospitalization remained unchanged. The mean peak CK declined 5% per year (p < 0.001), the proportion with abnormal enzymes declined 10% per year (p < 0.001), and the proportion that met criteria for definite (versus probable) MI declined 4% per year (p < 0.05). With stable hemodynamic indicators, worsening ECG indicators and improving enzymatic indicators, these results do not provide strong support for temporal changes in the severity of MI. The declines in peak CK levels, percentage with abnormal enzymes, and percentage with definite MI all support the conclusion that infarct size declined. These changes may be due to preventive efforts and/or to improvements in acute treatment (other than thrombolytic therapy) resulting in limitation of infarct size.

Temporal Trends in the Use of Anticoagulants among Older Adults with Atrial Fibrillation
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Background: Several recent randomized clinical trials have demonstrated that warfarin treatment, and to a lesser extent aspirin, reduces risk of stroke and death compared to placebo in atrial fibrillation. The extent to which the use of these therapies following trial publications has continued to increase in the elderly with atrial fibrillation is scantly documented. The extent to which the use of these therapies following trial publications has continued to increase in the elderly with atrial fibrillation is scantly documented. The purpose of this study was to examine trends in the use of anticoagulants in community dwelling older adults with atrial fibrillation. Methods: We used data from the Cardiovascular Health Study, a study of 5,888 community-dwelling adults 65 years of age or older, to determine the prevalence of warfarin and aspirin use in ECG-identified atrial fibrillation. ECG examinations were conducted at baseline, 1989-90, and at six subsequent annual examinations through 1995-1996. Medication data are collected by standard methods at each examination. Temporal trends in use of anticoagulants was analyzed by comparing percentage use in 1990 to use in each year through 1996. Results: The use of warfarin increased four-fold from 13% in 1990 to 50% in 1996 among participants with prevalent atrial fibrillation (p < 0.05). Daily use of aspirin did not increase over time. Participants <75 years of age were five times more likely to be using warfarin in 1996 compared to participants >75 years. Use of aspirin did not vary with age. Conclusions: Warfarin use in community-dwelling elderly persons with ECG-documented atrial fibrillation increased steadily following the first publication demonstrating a treatment benefit and reach 50% by 1996. In contrast, use of aspirin was unchanged during this same time period. Continued efforts to promote appropriate anticoagulation therapy to physicians and their patients are needed.

Paul G. McGovern, Donna K. Amett, Eyal Shahar, Russell V. Luepker, University of Minnesota, Minneapolis, MN.

The Minnesota Heart Survey is a surveillance study designed to document and explain trends in cardiovascular disease mortality, morbidity and risk factor levels in the Minneapolis-St. Paul metropolitan area. As part of this effort, serum total cholesterol (TC) was measured in population-based samples of area residents ages 25-74 years who attended a clinic visit in 1980-82 (N = 3,365), 1985-87 (N = 4,546), 1990-92 (N = 4,467) and 1995-97 (N = 4,095). All comparisons reported below are age-adjusted. Mean TC levels (mg/dL) declined dramatically in the 1980s from 212 in 1980-82 to 204 in 1990-92 in men, and from 208 in 1980-82 to 200 in 1990-92 in women (P < 0.001 for linear trend). However, there was no change in mean TC between 1990-92 and 1992-97 in either sex (P > 0.5). The prevalence of hypercholesterolemia (TC ≥ 200 mg/dL or antihyperlipidemic therapy) decreased in the 1980s in both sexes (P < 0.001), but increased between 1990-92 and 1995-97 in men (P = 0.05) and women (P = 0.11). This latter trend was due in part to increases in the prevalence of antihyperlipidemic medication use (2.6% in 1990-92 to 6.2% in 1995-97). WOMEN: 2.7% in 1990-92 to 3.7% in 1995-97. We conclude that the substantial population-wide reductions in the TC profile of Twin Cities adults observed during the 1980s have not continued in the 1990s.

Continued Declines in Cigarette Smoking: The Minnesota Heart Survey
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Trends in cigarette smoking prevalence, number of cigarettes smoked among smokers, and a biochemical marker of smoking, thiocyanate, were examined in the Minnesota Heart Survey, a population-based study of trends in cardiovascular disease risk factors. Cross-sectional surveys were done in 1980-82 (N=4061, 72.8% women), 1985-87 (N=3694, 72.9% women, 74.2% men), and 1990-92 (N=4581) in the Minneapolis-St. Paul metro area. Men and women, ages 25-74 years, completed home interviews regarding current and former smoking. Participants were invited to a fire station, where questions were asked about smoking patterns. Blood was collected for serum thiocyanate. The age-adjusted prevalence of current smoking, number of cigarettes smoked, and thiocyanate levels are listed in the Table for men (significance levels, t p < 0.01, + p < 0.05, - p > 0.05). Number of cigarettes smoked among current smokers also declined sharply from 1980-82 to 1995-97 (24.9/day versus 17.9/day in men, p < 0.01, 21.6/day versus 14.3/day in women, p < 0.01). Thiocyanate followed a similar pattern of decline, 79.6 versus 60.9 mg/dL in men (p < 0.01, 72.0 versus 61.0 mg/dL in women (p < 0.01). In conclusion, while these results indicate continued progress in smoking prevention and patterns of smoking among smoking, nearly 1 in 4 adults in the Twin Cities population still smoke, making it an issue of public health urgency.

Smoking Prevalence (%), # of cigarettes/day, and thiocyanate (nmol/d) by Survey Year
Survgy Year Prevalence # cig/day Thiocyanate
1980–82 35% 24.9 79.6
1985–87 32%* 22.8* 74.2*
1990–92 28%* 20.7* 64.9*
1995–97 23%* 17.9* 60.9*

Birth weight, breast feeding, and adolescent obesity.
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Background: Fetal and infant environment may influence development of obesity, a major determinant of CVD risk.

Methods: We analyzed data from 6415 girls and 5580 boys aged 9-14 yr in 1996, participants in a US cohort study of diet, activity, and growth, whose mothers (RN’s) reported birth weight/length and infant feeding practices. We defined obesity as body mass index >85th percentile for age and sex from NHANES I, 1971-74. We excluded premature births.

Results: Mean birth weight was 3.5 kg for girls, 3.4 kg for boys. In the first 6 months, 32% of subjects were breast fed only and 12% bottle fed only. At ages 9-14, 18% of girls and 26% of boys were obese. Adjusting for age, Tanner stage, menarche (girls), height, TV watching, and physical activity, the odds ratios and 95% CI’s for becoming obese were as shown in the Table (separate logistic model for each predictor). Breast feeding estimates were unchanged after adjustment for timing of introduction of formula, solids, or cow’s milk, none of which was an independent predictor of obesity.

Conclusions. Height, weight, and weight for length, at birth are associated with adolescent obesity. Breast feeding in the first 6 months of life and, possibly, increased duration of breast feeding appear to protect against development of obesity.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Girls OR (95% CI)</th>
<th>Boys OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (1 kg increment)</td>
<td>1.5 (1.3, 1.8)</td>
<td>1.2 (1.1, 1.4)</td>
</tr>
<tr>
<td>Birth ponderal index (hi v. lo quintile)</td>
<td>1.4 (1.1, 1.7)</td>
<td>1.2 (1.0, 1.5)</td>
</tr>
<tr>
<td>Breast feeding estimate (0-6 mo)</td>
<td>0.7 (0.6, 0.9)</td>
<td>0.8 (0.6, 1.0)</td>
</tr>
<tr>
<td>Breast feeding duration (3 mo increment)</td>
<td>0.97 (0.92, 1.02)</td>
<td>0.92 (0.88, 0.96)</td>
</tr>
</tbody>
</table>
Birthweight and blood pressure: The Fels Longitudinal Study.
Ellen Wochos Deemerlah, Bradford Towne, Shinu S. Goo, Winh Cameron Chu, Roger M. S. Vergroeff, Wright State University School of Medicine, Yellow Springs, OH

Background: The “fetal origins hypothesis” proposes that low birthweight increases the risk of cardiovascular disease (CVD) in later life. These findings, however, are based primarily on retrospective reports of birthweights. Given the numerous physiologic processes that intervene between birth and the adult onset of hypertension, it is appropriate to examine this hypothesis using a prospective study design.

Methods: The relationship between birthweight and blood pressure was examined in 345 individuals (166 males and 179 females) born between 1929 and 1967 who were followed from birth to mid-adulthood (mean age 45 years) in the Fels Longitudinal Study. Subjects were grouped by level of birthweight (“low” = lowest quartile; “high” = highest quartile; “average” = middle quartiles). Group differences in mean systolic and diastolic blood pressures at middle age were 120/76 in males and 109/68 in females. Mean systolic blood pressure was 5 mm Hg higher in low birthweight compared to the average birthweight group (p = 0.05).

Results: Mean systolic and diastolic blood pressures at middle age were 120/76 in males and 109/68 in females. Mean systolic blood pressure was 5 mm Hg higher in low birthweight compared to the average birthweight group (p = 0.05).

Conclusion: Low birthweight is associated with higher systolic blood pressure in mid-adulthood. This association, however, is mediated by the low birthweight in males of greater BMI after age 18 years.

11 Subclinical Atherosclerosis in Multiple Vascular Beds: An Index of Atherosclerotic Burden
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To evaluate extent of subclinical atherosclerosis, 153 postmenopausal women (mean age 59) underwent carotid ultrasound and electron beam CT of the coronaries and aorta resulting in measurement of aortic calcium (AC), coronary calcium (CC) and aortic calcification (AC). These four measures were highly correlated (Spearman), particularly IMP/2 (52, ACC/1.44) and ACP/40. For each measure, the 80th percentile was used as a cutoff to define the presence or absence of disease. The number of positive measures was then used as a subclinical disease scale (SDS) ranging from 0 to 3. No disease was found in 79 (52%) women, 33 (22%) were positive by 1 measure, 28 (18%) by 2 measures and 13 (8%) by 3 or 4 measures. Premonopausal risk factors were strongly associated with SDS. Mean HDL ranged from 62 in the no disease group to 49 for those at level 3 (p < 0.001). Logistic regression analysis was used to determine independent associations with SDS for the full group and stratified by hormone replacement therapy (HRT). Significant positive associations with SDS were HRT non-use (p < 0.002), Smoking (p = 0.054), and lower estrone (p = 0.002). Smoking ranged from 17% among those with no disease to 69% in those at level 3 (p < 0.001). Among the 74 women not on HRT, significant associations with SDS were higher LDL (p < 0.006) and lower estrone (p = 0.015). Among the 79 on HRT, significant associations were higher SBP (p = 0.02), smoking (p = 0.06), and older HDL2 (p = 0.002). In conclusion, for postmenopausal women, the number of vascular beds involved in subclinical atherosclerosis may be a powerful marker of future clinical events as a measure of atherosclerotic burden.

12 Dose-response relation of coronary artery calcification scores by electron beam computed tomography to coronary heart disease
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Several investigators report an association between coronary artery calcium (CAC) by electron beam computed tomography (EBCT) and coronary heart disease (CHD). However, it is unclear whether this association is present as a threshold or a dose-response relation. We investigated this issue in a large cross-sectional study of 7,334 persons aged 35 to 84 years, including 442 patients with known CHD. We classified study participants into five groups by their status and CAC scores: no CAC and quartiles (Q) 1 (score 1-15), Q2 (score 16-100), Q3 (score 101-417), and Q4 (score ≥418) of CAC scores. Compared with patients with no CAC, the odds ratios (95% confidence interval) for CHD for those in Q1, Q2, Q3, and Q4 were 7 (0.8-3.6), 4.6 (2.5-8.4), 10.5 (6.1-18.8), and 53.3 (32.9-93.1) after adjustment for age and sex (test for trend: p = 0.001). This trend extended to those in the highest 10%, 5%, and 1% of CAC scores; odds ratios were 10.8 (6.2-18.2), 12.0 (7.6-22.0), and 174.8 (85.3-357.4) respectively. A similar dose-response association was seen in women and men. In a subset of 852 patients with data on conventional risk factors, the odds ratios for CHD for participants in Q1, Q2, Q3, and Q4 were 3.3, 5.0, 9.3, and 51.0 (test for trend: p<0.0001) after adjustment for age, sex, current smoking, total cholesterol, high blood pressure, diabetes, and parental CVD. We saw no clear threshold for any cutpoint. CAC scores by EBCT may be a useful method for CHD risk stratification based on its strong dose-response association with CHD.
Coronary artery calcium scores correlate strongly between fast gated helical and electron beam computed tomography
J Jeffrey Carr, Gregorio L Burckart, David C Geff, John R Crouse, Ralph A D’Agostino, Wake Forest University School of Medicine, Winston-Salem, NC
Coronary artery calcium (CAC) is associated with coronary artery atherosclerosis as determined by pathologic and angiographic studies. CAC is a marker for coronary artery disease which may allow noninvasive and early detection of coronary atherosclerosis, as well as targeted interventions in high-risk individuals. The use of CAC in population-based studies has been limited by the lack of availability of electron beam computed tomography (EBCT) scanners. A new technology, fast-gated helical computed tomography (GFHCT) with subsecond scanning and ECG gating (480 msec temporal resolution) may make CAC testing widely available. We studied 33 participants with both EBCT (Siemens/Imatron) and GFHCT (General Electric) and obtained CAC scores using published thresholds for EBCT (130 HU for EBCT and 90 HU for GFHCT). The mean CAC means and ranges were 477.1 (0 to 3741) for EBCT and 557.6 (±3.868) for GFHCT. Total CAC scores with EBCT and GFHCT were highly correlated (Spearman correlation = 0.96, P < 0.0001). High risk for CHD was defined as a total CAC ≥ 200. Using this cutpoint, 30% (91% of 33 participants had complete agreement in CHD risk classification with EBCT & GFHCT. Of the 3 discordant CAC scores, 2 were high risk by EBCT and 1 by GFHCT. The discordant pairs likely represent variability across the 200-unit cutpoint. These data document the high correlation and concordance of CAC scores obtained with EBCT and GFHCT. Given the availability of helical CT scanners and their ability to detect CAC, the use of GFHCT technology may allow this noninvasive test for coronary atherosclerosis to be used in a greater number of settings. Incorporation of GFHCT into observational studies and trials will enhance understanding of the clinical and public health significance of CAC.

Mineralized carotid atherosclerosis on B-mode ultrasound predicts CHD: The Atherosclerosis Risk in Communities (ARIC) study
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We examined the relationship between carotid artery plaque (CAP), with and without acoustic shadowing (AOS) as an index of plaque mineralization, to incident CHD events in 12,375 men and women aged 45-64 years, free of CHD at baseline, examined in 1987-89 by the ARIC study. Over the course of 6 to 9 years of follow-up, 400 incident cases of MI or fatal CHD were identified and classified by a standardized protocol. Extracranial CAP was identified by B-mode ultrasound, and the presence of AOS was recorded, in each of six 1-cm arterial segments. A three level variable was defined based on the presence of arterial plaque and of AOS. After adjustment for age, race, and center, the hazard ratio (HR) of MI or fatal CHD for women with a CAP without AOS as compared to those without CAP was 2.31 (95% CI 1.5, 3.37), the HR compared with those with AOS with CAP to those with CAP without AOS was 2.21 (95% CI 1.9, 2.48), while the HR comparing those with a CAP with AOS to those with a CAP without AOS was 3.00 (95% CI 2.05, 4.12). The corresponding HRs for men were 1.8 (95% CI 1.2, 2.44), 1.22 (95% CI 0.72, 2.09) and 2.25 (95% CI 1.54, 3.30). Adjustment for diabetes, hypertension, cholesterol, smoking and fibrinogen attenuated these associations somewhat, but the HRs remained statistically significant for the comparisons including those free of CAP. The “established” CHD risk factors were predictive of incident CHD in the presence and absence of sub-clinical carotid atherosclerosis identified by B-mode ultrasound. In summary, CAP with and without AOS predicted CHD events, after adjustment for age, race and center, this association was statistically stronger for mineralized CAP in women, but not men. Further, recognized CHD risk factors remained important predictors of CHD in the presence of carotid plaque.

Lumbar Aortic Calcification is an Important Predictor of Vascular Morbidity and Mortality
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Depression as an antecedent to heart disease among men and women
Anty K. Ferketich, David J. Frid, Judith A. Schwartzbaum, The Ohio State University, Columbus, OH
Depression predicts morbidity and mortality among individuals who have coronary artery disease (CAD). However little is known about the effect of depression on the development of CAD. To evaluate depression as a precursor to heart disease we used data from the National Health and Nutrition Examination Survey, I (NHANESI). This analysis is based on the 5003 women and 2866 men who were free of CAD and completed the Center for Epidemiologic Studies Depression Scale (CES-D) at the 1982-84 interview. Scores of 16 or more and 23 or more have been suggested for “caseness” and “profound cases”, respectively. Using CAD incidence (ICD codes 410-414) as the outcome, a Cox proportional hazards regression was performed to evaluate the relative risk (RR) of CAD incidence in the depressed participants, controlling for confounders. There were 187 events among the males and 187 events among the females. The mean CES-D scores for the males and females were 7.3 ± 6.9 and 9.3 ± 8.8, respectively. Using a cut point of 16, the RR of CAD among the men was 1.69 (95% CI 1.3-2.5, p=0.012). Using the same cut point for women, the RR of CAD was 1.12, (95% CI 0.8-1.6, p=0.449). Because the women had higher baseline depression scores than the men, the cut point of 23 was then used to classify depression among women. Using this higher score, the RR increased to 1.78 (95% CI 1.2-2.8, p<0.010). Thus, depression has an independent effect on CAD incidence in both men and women, however, the effect in women is only seen at more severe levels of depression. The RR was unchanged after we deleted cases occurring within the first two years of observation, which suggests that the relation is not due to subclinical disease. Depression could possibly worsen serum lipids, or it may be related to CAD through heightened reactivity, often seen among depressed individuals.

The Impact of Becoming a Parent on Physical Activity: The CARDIA Study
Kathryn H Schmitz, David R Jacobs, Pam J Schreiner, Cote E Lewis, Carl J Caaspeton, Steve Sidney, Barbara A Kramar, CDC, Atlanta, GA, Kaiser Permanente, Oakland, CA, University of Alabama, Birmingham, AL, University of Minnesota, Minneapolis, MN

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Association between psychosocial factors and non-fatal cardiovascular disease in Mexican Americans and Non-Hispanic Whites
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Psychosocial factors such as type A behavior pattern (TyA) and anger (Ang) have been associated with increased risk of cardiovascular disease (CVD). However, few studies have examined these factors in Mexican Americans (MA). We investigated the associations of TyA and Ang with incident CVD using data from the San Antonio Heart Study (SAHS), a population-based study of CVD and diabetes in MA and non-Hispanic Whites (NHW) that included two exams 7-8 years apart. TyA and Ang were classified as at baseline using the Framingham 6-item TyA scale and the Spielberger Trait Anger scale. Incident CVD was defined as self-reported MI, heart surgery or stroke, angina by Rose Questionnaire, or death due to CVD among persons without CVD at baseline. Logistic regression (LR) was used to test whether becoming a parent was associated with a reduction in self-reported PA among young adults, with particular comparisons across gender, race, and marital status. Leisure-time PA, parental and marital status were reported 5 times over 10 years in a population based sample of 3274 black and white men and women, aged 18-30 at baseline. Frequency and intensity of PA were used to determine exercise units (EU). 50 EU is equivalent to jogging less than 2 hours weekly for 6 out of a year. PA associated with child care was not considered in this analysis. Repeated measures regression predicted change in PA from change in parenting status (3 levels: 0, 1, or 2 children), adjusting for marital job status, age, education, smoking, alcohol, and BMI. The results in the table suggest that becoming a parent was associated with reduced PA in women, but not in men. The association was stronger in white than black women (p<0.0001). Becoming the parent of more than one child did not enhance change in PA for any sub-group. Among all sub-groups, being married was independently associated with reduced PA (p<0.01), although marital status did not significantly modify the parenting and PA association (p=0.32). Time spent caring for children may partly explain why women commonly report being more tired than men, however it is not due to subclinical disease. Depression could possibly worsen serum lipids, or it may be related to CAD through heightened reactivity, often seen among depressed individuals.
Hostility Predicts Coronary Artery Calcification in Young Adults: the CARDIA Study

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High hostility levels have been found to be associated with several manifestations of coronary heart disease. This study examined the relationship of hostility (measured using the Cook & Medley Hostility Scale [CMHS]) with coronary calcification, a subclinical measure of atherosclerotic coronary disease. Participants were 376 men and women, aged 18-30 at baseline, who underwent electron-beam computed tomography (EBCT) as part of the Year 10 exam (1995) of the biracial CARDIA (Coronary Artery Risk Development in Young Adults) cohort. In sex-race-age adjusted logistic regression analysis and compared to those in the lowest tertile (≤15 points), those in the upper tertile of the CMHS measured at baseline in 1985 (≥23 points) were more likely to have coronary calcification defined as a Total Agatston Calcium Score ≥20 units (≥n=19, odds ratio=2.9, 95% confidence interval, 1.7-4.5). A 1.6 difference in CMHS at baseline (8.1 points) was associated with 2.0 higher odds (95% confidence interval, 1.1-3.8) of coronary calcification. Although to a lesser extent, hostility measured in the Year 5 exam (1990) continued to predict coronary calcification, the 5-year change in hostility did not affect. Based for adjustment for sex-race strata, the relationship between hostility and coronary calcification was predominantly seen in white men. We conclude that high hostility may be associated with early development of coronary artery calcification detected using EBCT. Also, this association was independent of traditional behavioral and biological coronary risk factors.

Effect of Soy Protein and Phytosterol Intake on Plasma Lipids in Hypercholesterolemic Postmenopausal Women

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Background: It has been suggested that phytosterols derived from soy beans may have a hypocholesterolemic effect. However, evidence to substantiate this claim is limited. Design: Randomized, double-blind, placebo-controlled, clinical trial, with a parallel design. Ninety-four postmenopausal, hypercholesterolemic (LDL-C 150 ± 23 mg/dL, mean ± SD, range 130-190 mg/dL) women were randomized to receive a powered protein supplement with 40 grams of protein and 240 mg of sodium (MILK), 120 mg of protein with trace phytosterols (SOY-trace), or 3 soy protein with 145 mg of phytosterol (isoflavone) per day (SOY-Iso145). Duration: One-month run-in with milk protein, followed by 3-month randomization period.

Outcomes: Plasma lipoprotein cholesterol and triglycerides.

Results: There were no significant differences between MILK and either SOY-trace, or SOY-Iso145. Total cholesterol decreased significantly more among SOY-Iso145 than among SOY-trace.

Conclusion: These findings do not support a cholesterol-lowering effect of soy protein, or without phytosterols, relative to milk protein in postmenopausal, hypercholesterolemic women. Phytosterogen intake may be warranted for other health outcomes.

Risk of Early-Onset Myocardial Infarction Associated With Decreased Low Density Lipoprotein Size in Women

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Previous studies of middle-aged men and women have shown an association between low density lipoprotein (LDL) particle diameter (size) and the occurrence of myocardial infarction (MI). However, this association has yet to be examined in younger women. In a sub-sample from a population-based case-control study of women living in Western Washington, we examined the association between LDL size and risk of early-onset MI. Gradient gel electrophoresis was utilized to evaluate LDL size in non-fasting plasma samples from 72 MI cases and 159 controls 20-44 years of age. Cases had significantly smaller mean LDL size (26.4 ± 0.8 nm) than controls (26.9 ± 0.7 nm) (p<0.001). The association indicated that for every 0.1-nm decrease in LDL size in nanometers (nm), the risk for CVD increased by 23% (OR=1.23, 95% CI=1.10-1.38). After controlling for menopause, smoking, and BMI the OR decreased to 23% (OR=0.77, 95% CI=0.64-0.94). Although we did not detect a significant interaction between soy intake and diabetes status, no significant risk was detected for soy intake among the lowest serum folate tertile were statistically lower when compared with those excluded (RR=1.04, RR=0.04, RR=0.62 and RR=0.85) among all participants and excluding those who reported CVD at baseline, respectively. Although we did not detect a significant interaction between soy intake and diabetes status, no significant risk was detected for soy intake among the lowest serum folate tertile.
Familial Aggregation of Systemic Inflammatory Markers: The NIHHLI Family Heart Study
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Prospective studies indicate that systemic markers of inflammation measured at baseline are associated with increased risk of coronary heart disease, stroke, and peripheral vascular disease, but the conditions promoting this inflammatory response have not been clarified. We assessed familial aggregation of three inflammatory markers (leukocyte count, albumin, and C-reactive protein) in probability selected families from U.S. communities. We estimated gender- and age-adjusted familial correlations for parent-child, sibling, and spouse pairs (table). Evidence for familial aggregation was stronger in biological relatives. Sexually dimorphic effects of familial and genetic influences on these systemic markers of inflammation. Compared to never smokers, leukocyte, albumin, and CRP levels in current smokers were 25% higher, 1% lower, and 29% higher, respectively; however, familial correlations were not substantially different across these restricted to never smokers. These data suggest that first-degree relatives may experience a similar systemic inflammatory response because of shared genes or environmental factors.

Familial correlations (p-value) by relative pair:

<table>
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<tr>
<th>Inflammatory Marker</th>
<th>Parent-child</th>
<th>Sibling</th>
<th>Spouse</th>
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<tr>
<td>Leukocytes</td>
<td>0.19 (p = 0.01)</td>
<td>0.20 (p = 0.001)</td>
<td>0.04 (p = 0.46)</td>
</tr>
<tr>
<td>Albumin</td>
<td>0.13 (p = 0.001)</td>
<td>0.18 (p &lt; 0.001)</td>
<td>0.04 (p = 0.41)</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>0.55 (p &lt; 0.001)</td>
<td>0.27 (p &lt; 0.001)</td>
<td>NA*</td>
</tr>
</tbody>
</table>

* CRP was measured only on biological relatives.

Markers of inflammation and risk of myocardial infarction in an elderly population: The Rotterdam study
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Background: Low-level, chronic inflammation is involved in the process of atherogenesis and may predict risk of coronary heart disease. We examined the relation between measures of inflammation and risk of myocardial infarction in an elderly population.

Methods: The associations were examined in the Rotterdam study, a prospective population-based study among 7983 subjects aged 55 years and older and living in Rotterdam, The Netherlands. Inflammation was measured by levels of the acute phase proteins C-reactive protein and C-reactive protein (CRP). We selected the first 111 cases of myocardial infarction, which were age- and sex-matched with controls who remained free from the disease during follow-up.

Results: Relative risks of myocardial infarction for increasing quartiles of c-reactoprotein were 1.1 (95% confidence interval 0.5-2.4), 1.5 (0.7-3.3) and 3.0 (1.6-5.8), respectively, compared to the lowest quartile. Adjustment for other cardiovascular risk factors only slightly changed the estimates. The relative risks were most evident among current smokers: 1.2 (0.5-1.9), 3.5 (0.4-38) and 9.1 (1.4-48), respectively, for increasing quartiles of c-reactoprotein compared to the lowest quartile. No effect modification was observed for other cardiovascular risk factors. Sixty-five percent of the population had a CRP value below the detection level. Subjects with a CRP level above 6 g/L had a 2.7 (1.3-5.9) times increased risk of myocardial infarction adjusted to subjects with lower levels.

Conclusion: The results of this prospective, population-based study show that inflammation markers are strong predictors of myocardial infarction in an elderly population. The risk estimates are highest among current smokers.

The Relationship of C-Reactive Protein to the Incidence of Thromboembolic Stroke
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There is little prospective data available on the relationship of C-reactive protein to the incidence of stroke. Utilizing a nested case-control design, the relationship between C-reactive protein, and subsequent risk of fatal plus non-fatal thromboembolic stroke over an average 21 year follow-up period, was evaluated in 4274 former and never-smoking participants in Honolulu.

Results: CRP levels were 0.38(0.39) mg/dl in 1500 controls, 0.18 (p < 0.0003) mg/dl in those with diabetes mellitus, 0.38 (p < 0.0003) mg/dl in those with hypertension and had significantly higher serum cholesterol, serum glucose, body mass index and cigarettes per day than controls. Among both younger (46-55) and older (56-70) men as well as among never smokers, those in the third tertile of C-reactive protein had significantly higher age-adjusted rates of thromboembolic stroke. A similar non-significant trend was seen for current smokers. The age-adjusted percent of men experiencing a thromboembolic stroke ranged from 11.2% in the first tertile of C-reactive protein to 19.9% in the third tertile. The risk factor adjusted relative risk of thromboembolic stroke was 1.5 (p = 0.059/95% confidence interval 1.0-2.2) for the third tertile of C-reactive protein, compared to the first tertile. Among never smokers the relative risk was 4.7 (p < 0.001/95% CI 2.0-11.3), while for current smokers it was 1.8 (non-significant). The relative risk was 2.2 (p < 0.05/95% CI 1.2-4.2) in men of 48-55 and 1.2 in those 56-70 (non-significant). Thus, baseline C-reactive protein level was strongly related to the incidence of thromboembolic stroke in this population over an extended follow-up period. This relationship was strongest in middle aged men and in those who had never smoked.

C-reactive protein and risks of myocardial infarction, stroke and death in an elderly cohort
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Background: Inflammation markers such as C-reactive protein (CRP), and measures of subclinical cardiovascular disease (CVD) are risk factors for major cardiovascular disease. We assessed the relationship of CRP to CVD in a prospective cohort study of elderly men enrolled in the Honolulu Heart Program cohort. There were 259 cases of thromboembolic stroke and 1348 controls without coronary heart disease or stroke during the follow-up. Risk factor combinations were more common in controls. Thus, cases had significantly more hypertension and had significantly higher serum cholesterol, serum glucose, body mass index and cigarettes per day than controls. Among both younger (46-55) and older (56-70) men as well as among never smokers, those in the third tertile of C-reactive protein had significantly higher age-adjusted rates of thromboembolic stroke. A similar non-significant trend was seen for current smokers. The age-adjusted percent of men experiencing a thromboembolic stroke ranged from 11.2% in the first tertile of C-reactive protein to 19.9% in the third tertile. The risk factor adjusted relative risk of thromboembolic stroke was 1.5 (p = 0.059/95% confidence interval 1.0-2.2) for the third tertile of C-reactive protein, compared to the first tertile. Among never smokers the relative risk was 4.7 (p < 0.001/95% CI 2.0-11.3), while for current smokers it was 1.8 (non-significant). The relative risk was 2.2 (p < 0.05/95% CI 1.2-4.2) in men of 48-55 and 1.2 in those 56-70 (non-significant). Thus, baseline C-reactive protein level was strongly related to the incidence of thromboembolic stroke compared to the first tertile. Among never smokers the relative risk was 4.7 (p < 0.001/95% CI 2.0-11.3), while for current smokers it was 1.8 (non-significant). The relative risk was 2.2 (p < 0.05/95% CI 1.2-4.2) in men of 48-55 and 1.2 in those 56-70 (non-significant). Thus, baseline C-reactive protein level was strongly related to the incidence of thromboembolic stroke in this population over an extended follow-up period. This relationship was strongest in middle aged men and in those who had never smoked.

Relationships of C-Reactive Protein and Lipoproteins to Plasma Fibrinogen Levels
Stephen B Kritchevsky, Andrew J Bush, Marco Pahor, Myron D Gross, University of Washington, Seattle, WA, Wake Forest University, Winston-Salem, NC

Several studies have found that serum carotenoids are inversely associated with cardiovascular disease risk. To date, however, supplementation trials of -carotene have shown no benefit. To determine whether inflammation might confound the epidemiologic relationships we related the levels of -carotene (AC; mean(SD): 0.00(0.13) mg/mL), -carotene (BC; 0.38(0.39) mg/mL), -cyanocarotin (CC; 0.21(0.16) mg/mL), lycopene (LY; 0.45(0.20) mg/mL, and ascorbic acid (AA; 0.42(0.23) mg/mL) and serum c-reactive protein (CRP; 0.28(0.69) mg/dl), fibrinogen (FB; 2.80(7.5) g/L), and white blood cell count (WBC; 6.62(8.7) x 109/L), in 4,557 former and never-smoking participants aged 25-55 in the Third National Health and Nutrition Survey. The group study was 60% female, 30% African-American, 33% Hispanic. Using ANCOVA to adjust for gender, age, body mass index, income, education, smoking status, and alcohol consumption, total serum cholesterol, HDL cholesterol, dietary supplement use and self-reported health status, all 5 of the measured carotenoids were significantly lower in participants with CRP levels over 0.88 mg/dl (the 95th percentile) compared to levels below 0.21 mg/dl (the 95th percentile): p < 0.005). AC and BC were 20% lower while the other 3 carotenoids ranged between 7.9% lower. There were no differences in mean carotenoid concentrations by quartile of fibrinogen level. There was a modest inverse association between BC and WBC (p value for linear trend across quartiles of WBC = 0.04) which became more pronounced after log-transforming BC (p trend <0.01) with those with WBC over 7.85 (the upper quartile) having significantly lower log-BC (p < 0.05) than those with WBC below 6.55 (the median). The association between log-BC and WBC was independent of CRP. Log transformation did not affect associations between other carotenoids and inflammatory markers. No interactions with smoking use or health status were observed. These data suggest that inflammation is related to the metabolism of carotenoids, and that markers of inflammation may be important confounders of carotenoid-CVD relationships.