

[연수강좌]

미세영양소의 임상적 적용

조 비 룡

서울의대 가정의학교실

강의 내용

- Homocystein related Vitamin B complex
- Vitamin D
 - With Calcium
- Multivitamin
- Antioxidant (Vitamin)
- Phytochemical

1. Homocysteine associated Vitamins

- Vitamin B₆ (pyridoxin)
- Vitamin B₉ (folacin)
- Vitamin B₁₂ (cobalamin)
- Betaine, Cholin

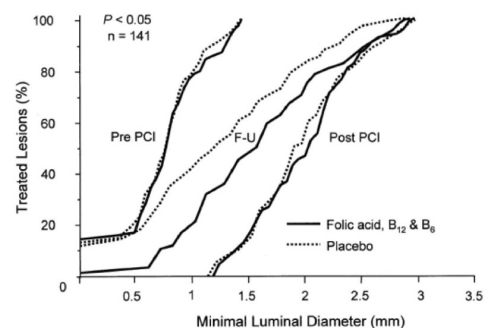
Effect of Homocysteine-Lowering Therapy on Restenosis After Percutaneous Coronary Intervention for Narrowings in Small Coronary Arteries

Guido Schnyder, MD, Marco Roffi, MD, Yvonne Flammer, MD, Riccardo Pin, MD, Franz R. Eberli, MD, Bernhard Meier, MD, Zoltan G. Turi, MD, and Otto M. Hess, MD

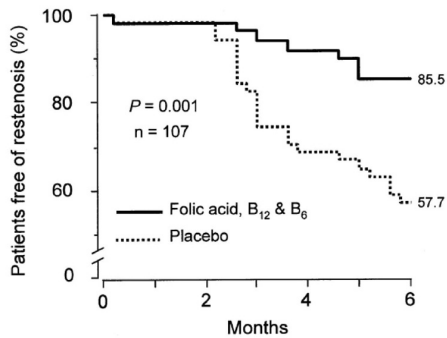
(2003, AJC)

- 58/55 RCT
- Homocysteine-lowering 치료가 PCI 이후의 Small Coronary A.의 협착을 유의하게 줄인다.
 - RR = 0.34

6개월 후의 MLD의 변화 비교



Freedom from Restenosis



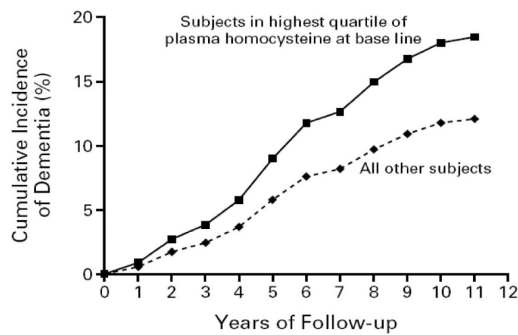
The New England Journal of Medicine (2000, 2)

PLASMA HOMOCYSTEINE AS A RISK FACTOR FOR DEMENTIA AND ALZHEIMER'S DISEASE

SUDHA SESHADRI, M.D., ALEXA BEISER, Ph.D., JACOB SELHUB, Ph.D., PAUL F. JACQUES, Sc.D., IRWIN H. ROSENBERG, M.D., RALPH B. D'AGOSTINO, Ph.D., PETER W.F. WILSON, M.D., AND PHILIP A. WOLF, M.D.

- 1092명 (평균 76세) Retrospective 관찰
- Framingham Study
- 높은 Homocysteine 농도는 AD의 강력한 위험 인자
- OR 1.4/SD/8 year
- Hyperhomocysteinemia (>14umol/L)
- Risk Double

Crude Cumulative Incidence of Dementia



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 13, 2004 VOL. 350 NO. 20

Homocysteine Levels and the Risk of Osteoporotic Fracture

Joyce B.J. van Meurs, Ph.D., Rosalie A.M. Dhonukshe-Rutten, M.Sc., Saskia M.F. Pluijm, Ph.D., Marjolijn van der Klift, M.D., Ph.D., Robert de Jonge, Ph.D., Jan Lindemans, Ph.D., Lisette C.P.G.M. de Groot, Ph.D., Albert Hofman, M.D., Ph.D., Jacqueline C.M. Witteman, Ph.D., Johannes P.T.M. van Leeuwen, Ph.D., Monique M.B. Breteler, M.D., Ph.D., Paul Lips, M.D., Ph.D., Huibert A.P. Pols, M.D., Ph.D., and André G. Uitterlinden, Ph.D.

- 2406 Cohort Study, 3 Group
- Hyperhomocysteinemia는 Osteoporotic fracture의 독립적인 위험요인이다.
- RR = 1.4/SD

Cumulative Incidence of Fracture

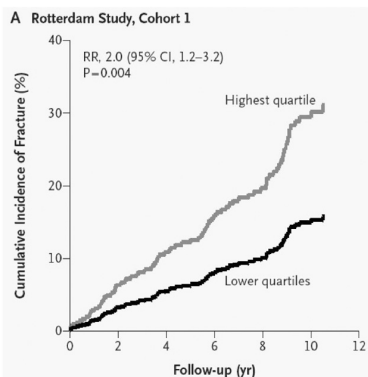
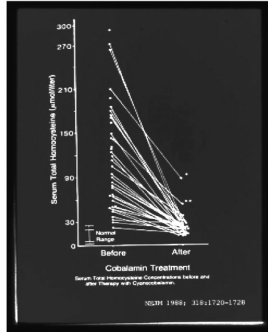


Table 4. Relative Risks and Population Attributable Risks for Independent Risk Factors for Incident Fracture.*

| Factor | Relative Risk (95% CI) | Population Attributable Risk (95% CI) |
|--------------------------------------|------------------------|---------------------------------------|
| | | % |
| Age >75 yr | 2.3 (1.7-3.1) | 31 (25-48) |
| BMD, lowest quartile | 1.6 (1.1-2.3) | 13 (2-25) |
| Current smoker | 1.6 (1.1-2.3) | 10 (4-23) |
| Fall in previous year† | 1.9 (1.2-2.7) | 20 (10-35) |
| Dementia and cognitive impairment† | 2.5 (1.5-4.1) | 15 (7-30) |
| Homocysteine level, highest quartile | 1.9 (1.4-2.6) | 19 (10-29) |

'Marginal' B12 deficiency can result in neurodegenerative diseases

- 141 subjects with a variety of neurodegenerative diseases whose disease significantly improved with administration of B12
- A significant minority of these subjects had 'low-normal' B12 levels of 200-350 pg/mL



Homocystein의 기대 기능

- 동맥 경화 방지
 - 심혈관계 질환 예방
- 치매 예방
- 말초 신경질환 예방
- 골절 예방

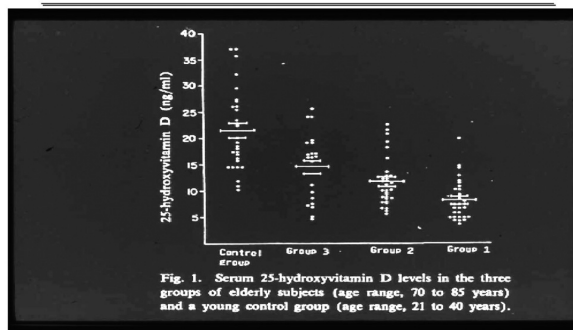
Vit B Treatment Protocol

- Folic acid (0.4 -5 mg)
 - 4주 투여 시 약 25% 감소
- Vitamin B₁₂ (200-1000 µg)
 - 7% 추가 감소
- Pyridoxine (10 - 250 mg)

강의 내용

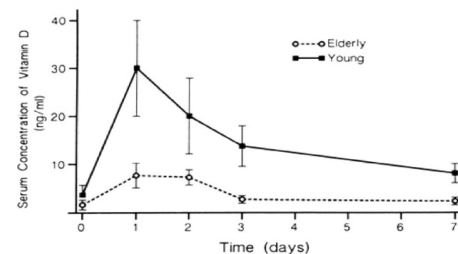
- Homocystein related Vitamin B complex
- Vitamin D
 - With Calcium
- Multivitamin
- Antioxidant (Vitamin)
- Phytochemical

2. Vitamin D levels diminish with age and disability



Causes of diminished D levels in the elderly

- habitually low dietary intake (120 I.U./d)
- impaired synthesis in senile skin (see below)
- little sun exposure in homebound and institutionalized elders



Vit. D effects on Fall

Moderate protective effect on Fracture Risk

– Bone Mineral Density change

Effects of a Short-Term Vitamin D and Calcium Supplementation on Body Sway and Secondary Hyperparathyroidism in Elderly Women

MICHAEL PFEIFER¹, BETTINA BEGEROW¹, HELMUT W. MINNE¹, CHRISTINE ABRAMS², DETLEF NACHTIGALL³ and CORINNA HANSEN⁴

¹Institute of Clinical Osteology "Gustav-Pommerehne" and Clinic "DER FORSTENHOF", Bad Pyrmont, Germany;
²Department of Public Health and Primary Care, University of Hull, Hull, U.K.;
³Stathmann Company, Hamburg, Germany.

- 148 women (mean [±SD] age, 74 ± 1 years)
- 25-hydroxycholecalciferol level below 50 nmol/liter
- Supplementation : 8주간 시행
 - 1200 mg of calcium plus 800 IU of vitamin D
 - 1200 mg of calcium
- 결과
 - a decrease in the serum PTH of 18% ($p = 0.0432$)
 - a decrease in body sway of 9% ($p = 0.0435$)
 - mean number of falls per subject during a 1-year follow-up period
 - 0.45 for the calcium mono group
 - 0.24 for the calcium and vitamin D group ($p = 0.0346$).

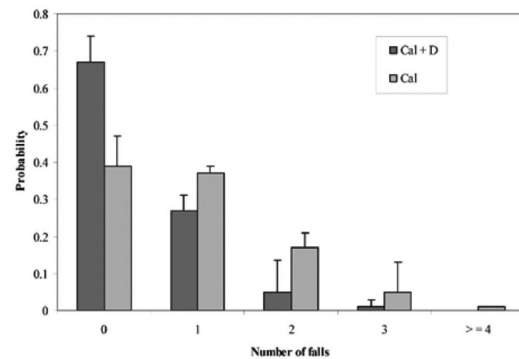
Effects of Vitamin D and Calcium Supplementation on Falls: A Randomized Controlled Trial

HEIKE A. BISCHOFF^{1,2}, HANNE S. STAHELIN³, WALTER DICK¹, REGULA AKOS¹, MARGRITH KNECHT³, CHRISTIAN SALUS¹, MATTHIAS NEUBER¹, ROBERT THEILER⁴, MICHAEL PFEIFER⁵, BETTINA BEGEROW⁶, ROBERT A. LEW² and MARTIN CONZELMANN⁶

¹Department of Orthopaedics, University of Basel, Basel, Switzerland; asid5911951
²Division of Rheumatology, Immunology and Allergy, The Robert B. Brigham Multipurpose Arthritis Center, Brigham and Women's Hospital, Boston, Massachusetts, USA
³Department of Geriatrics, University of Basel, Basel, Switzerland
⁴Department of Rheumatology, University of Basel, Basel, Switzerland
⁵Institute for Clinical Osteology, Bad Pyrmont, Germany
⁶Department of Geriatrics, Felix Platter Spital, Basel, Switzerland

- 122 elderly women (mean age, 85.3 years) in long-stay geriatric care.
 - 1200 mg calcium plus 800 IU cholecalciferol ($n = 62$)
 - 1200 mg calcium ($n = 60$)
- 12-week treatment period.
- 결과
 - Falls per person (0, 1, 2-5, 6-7, >7 falls)
 - Musculoskeletal Function
 - TUG test, knee flexor/extensor strength, grip strength.

Vitamin D & Fall



Vitamin D on Musculoskeletal Function

TABLE 5. MUSCULOSKELETAL FUNCTION AT BASELINE AND PERCENTAGE DIFFERENCE FROM BASELINE AFTER 3 MONTHS OF FOLLOW-UP IN THE TWO TREATMENT GROUPS

| Characteristics | Baseline (n = 60 in Cal-group and n = 62 in Cal + D-group) | | Change (n = 29 in Cal-group and n = 33 in Cal + D-group) | |
|----------------------------------|--|-------------|--|-------------|
| | Median (IQR) | p Value (1) | Percentage change | p Value (2) |
| Knee flexor strength (kp)* | | | | |
| Cal-group | 8.0 (5.5–10.0) | | –3.9% | |
| Cal + D-group | 7.5 (6–9.9) | NS | +3.7% | |
| Knee extensor strength (kp)* | | | | |
| Cal-group | 11.75 (9.25–15.5) | | +1.4% | |
| Cal + D-group | 12.5 (9.63–15.5) | NS | +8.6% | |
| Grip strength (bar)* | | | | |
| Cal-group | 0.190 (0.155–0.263) | | +0% | |
| Cal + D-group | 0.205 (0.130–0.265) | NS | +5.5% | |
| Timed up & go test(s) | | | | |
| Cal-group | 23 (17–39.5) | | –3.2% | |
| Cal + D-group | 25 (19.5–40.5) | NS | –11.1% | |
| Overall musculoskeletal function | | | | 0.0094 |

p value (1) represents the probability of the difference of the median baseline values between the two treatment groups in 122 subjects. IQR represents interquartile range. Change shows difference from baseline in percent (based on median changes) among 62 subjects who had complete data set at baseline and follow-up for single measurements. p Value (2) represents the probability of the difference of change between the two treatment groups over time for overall summed musculoskeletal function.

* To convert kilopond into Newton multiply by 10.

† One bar equals 10³ pascal, which is equivalent to 1 N/m².

Vit. D effects on Fall

Moderate protective effect on Fracture Risk

- Bone Mineral Density change
- Directly improve Muscle Strength
 - Reducing Fx. Risk through fall prevention
 - Reduced Fx. within 8 to 12weeks

Effect of Vitamin D on Falls A Meta-analysis

Heike A. Bischoff-Ferrari, MD, MPH
Bess Dawson-Hughes, MD
Walter C. Willett, MD, DrPH
Hannes B. Staehelin, MD
Marlet G. Bazemore, MD
Robert Y. Zee, MD
John B. Wong, MD

Context Falls among elderly individuals occur frequently, increase with age, and lead to substantial morbidity and mortality. The role of vitamin D in preventing falls among elderly people has not been well established.

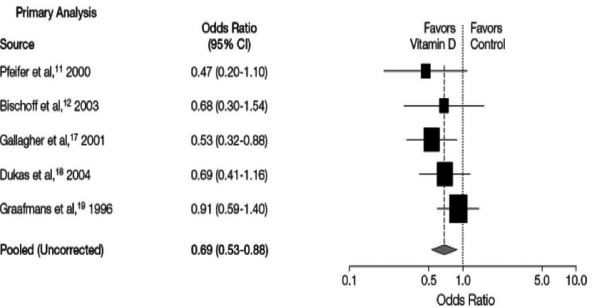
Objective To assess the effectiveness of vitamin D in preventing an older person from falling.

Data Sources MEDLINE and the Cochrane Controlled Trials Register from January 1960 to February 2004, EMBASE from January 1991 to February 2004, clinical experts, bibliographies, and abstracts. Search terms included trial terms: *randomized-controlled trial or controlled-clinical trial or random-allocation or double-blind method, or trials, blind method or uncontrolled trials with vitamin D or vitamin D deficiency or*

• JAMA 2004;291:1999-2006

• Vit D의 낙상에 대한 효과에 대한 Meta-analysis

Results Primary Analysis



Comment

- 22% reduction in the risk of falling
 - compared with Calcium or placebo
 - NNT = 15
- Muscular Effect of Vitamin D
 - Type II muscle fiber hypertrophy after 3 mos.
 - Nuclear Vit D receptor 가 근육에 풍부하게 존재

JAMA

the American Medical Association. All Rights Reserved. Applicable FARS/DIARS Restrictions Apply to Government Use. American Medical Association, 515 N. Dearborn St., Chicago, IL 60610.

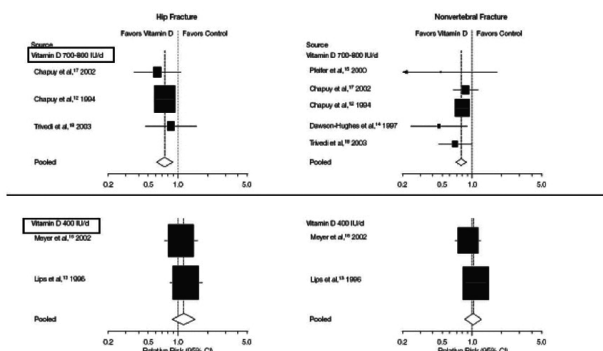
Volume 293(18) 11 May 2005 p 2257-2264

Fracture Prevention With Vitamin D Supplementation: A Meta-analysis of Randomized Controlled Trials [Review]

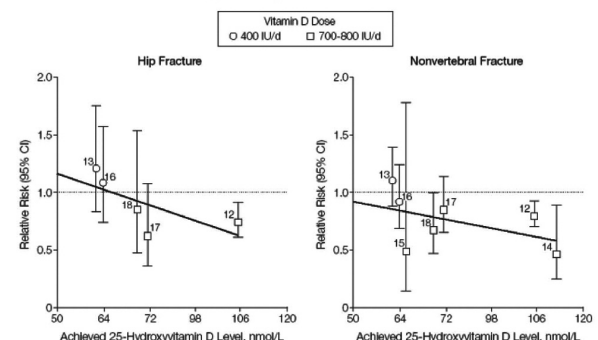
Bischoff-Ferrari, Heike A. MD, MPH, Willett, Walter C. DrPH, Wong, John B. MD, Giovannucci, Edward ScD, Dietrich, Thomas MPH, Dawson-Hughes, Bess MD

- SR
 - 5 RCT for Hip Fx(9294), 7 RCT for nonvertebral Fx (9820)
- Results
 - Vit D 전체적인 효과는 없다
 - 700IU – 800IU : RR (Hip Fx) = 26%
RR (NonV Rx) = 23%

Forest Plots Comparing the Risk of Hip and Nonvertebral Fractures



Hip and Nonvertebral Fracture Efficacies by Achieved 25-Hydroxyvitamin D Levels



Effects of Vitamin D on Disease

- 골다공증
 - 뼈의 칼슘 침착
- 암
 - 전립선, 대장, 유방
 - 세포 분화 유도, 세포 증식 억제
- Autoimmune ds.
 - 과량 또는 결핍시 문제
- 근육 기능 향상

Vitamin D 권장안

- 50세 이하 : 200 IU
- 50세 - 70세 : 400 IU
- 70세 이상 : 600 IU
 - 근육 기능향상 : 800 IU
- 일주일에 3일 이상 15분씩 일광욕
- UL : 2000 IU
 - 혈중 칼슘 증가에 의한 부작용

Reducing tooth loss in the elderly with vitamin D+calcium supplementation

- A randomized, controlled trial (described in the prior slide: 145 elder subjects, 3 yr. intervention with D+calcium)
- Detailed dental exams were performed
- Results:
 - 13% in the Ca/D group vs. 27% in placebo group lost one or more teeth over 36 mos.
 - Odds of tooth loss=0.4 (C.I. 0.2-0.9)
 - Effects did not differ by gender or by smoking status

Am J Med 01:111:452-456

강의 내용

- Homocystein related Vitamin B complex
- Vitamin D
 - With Calcium
- Multivitamin
- Antioxidant (Vitamin)
- Phytochemical

CLINICAL INVESTIGATIONS

3. Multivitamin

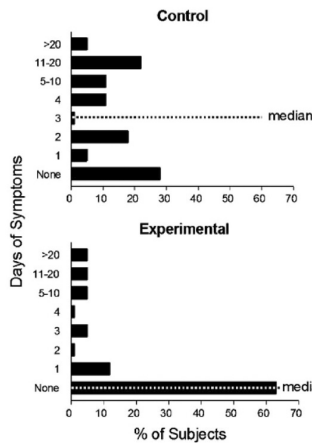
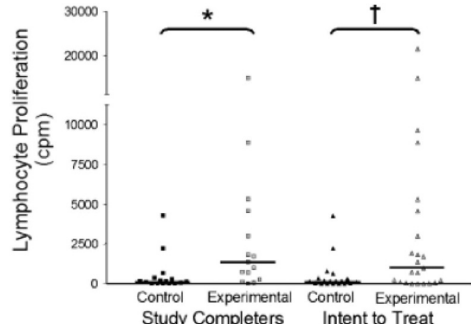
Nutritional Formula Enhanced Immune Function and Reduced Days of Symptoms of Upper Respiratory Tract Infection in Seniors

Bobbi Langkamp-Henken, PhD,* Bradley S. Bender, MD,* Elizabeth M. Gardner, PhD,*⁸⁰ Kelli A. Herringer-Garcia, BS,* Michael J. Kelley, PhD,* Donna M. Murasko, PhD,*⁸¹ Joseph P. Schaller, PhD,* Joyce K. Stechmüller, PhD,* Debra J. Thomas, MS,* and Steven M. Wood, PhD*

- Prospective, double-blind, RCT
 - > 65 yr old, 66명
- 8 oz/d experimental formula
- Outcome : ① URI, ② Ab titer, ③ Lymphocyte proliferation to influenza vaccination components

사용된 Nutrient Composition

| Nutrient | RDA or AI* | Experimental Formula ¹ | Control Formula ² | Vitamin/Mineral Supplement ³ |
|------------------------------|------------|--|--|--|
| Energy, kcal | | 360 | 360 | NA |
| Protein, g (% energy) | | 13 (15) | 13 (15) | NA |
| Carbohydrate, g (% energy) | | 49 (55) | 49 (55) | NA |
| Fat, g (% energy) | | 13 (30) | 13 (30) | NA |
| Vitamin A, µg ⁴ | 900 | 259 | - | 600 |
| Vitamin D, µg | 15 | 2 | - | 5 |
| Vitamin E, mg | 15 | 103 | - | 3 |
| Vitamin K, µg | 120 | 11 | - | - |
| Vitamin C, mg | 90 | 281 | - | 30 |
| Folic acid, µg | 400 | 361 | - | - |
| Thiamine, mg | 1.2 | 2.1 | - | 1.5 |
| Riboflavin, mg | 1.3 | 2.0 | - | 1.5 |
| Vitamin B ₆ , mg | 1.7 | 2.0 | - | 1.5 |
| Vitamin B ₁₂ , µg | 2.4 | 7.1 | - | 5 |
| Niacin, mg ⁵ | 16 | 16 | - | 1 |
| Choline, mg | 550 | 118 | - | - |
| Biotin, µg | 30 | 284 | - | - |
| Pantothenic acid, mg | 5 | 10 | - | 2 |
| Calcium, mg | 1,200 | 204 | 42 | 1.5 |
| Phosphorus, mg | 700 | 204 | 129 | - |
| Magnesium, mg | 420 | 76 | 5.7 | 0.3 |
| Iodine, mg | 0.15 | 0.05 | - | 0.02 |
| Copper, mg | 0.9 | 0.8 | 0.2 | 0.1 |
| Zinc, mg | 11 | 58 | 1 | - |
| Iron, mg | 8 | 4 | - | 1 |
| Selenium, µg | 55 | 62 | 6 | - |
| Chromium, µg | 30 | 29 | - | - |
| Molybdenum, µg | 45 | 48 | - | - |
| Beta-carotene, mg | | 8 | - | - |
| Taurine, mg | | 67 | - | - |
| Carnitine, mg | | 59 | - | - |
| Osmolality, mosm/kg | | 650 | 550 | NA |
| Protein source | | 73% sodium caseinate, 11% calcium caseinate, 16% soy protein isolate | 73% sodium caseinate, 11% calcium caseinate, 16% soy protein isolate | 80% casein, 10% soy protein isolate |
| Fat source | | 68% structured triacylglycerol (60/20/20 ratio), 14.5% high oleic safflower oil, 14.5% soybean oil, 2% soy lecithin (emulsifier) | 87% corn oil, 3% soy lecithin (emulsifier) | 87% corn oil, 3% soy lecithin (emulsifier) |
| Carbohydrate source | | 71% maltodextrin, 20% sucrose, 9% hydrolyzed gelatin | 77% maltodextrin, 20% sucrose | 77% maltodextrin, 20% sucrose |



bmj.com

Role of multivitamins and mineral supplements in preventing infections in elderly people: systematic review and meta-analysis of randomised controlled trials

Alia El-Kadiki and Alexander J Sutton

BMJ 2005;330:871-; originally published online 31 Mar 2005;
doi:10.1136/bmj.38399.495648.8F

- Systematic Review
- 8 Clinical Trials were included
- Results
 - 연중 평균 감염 일수 = 17.5% 감소 (11 - 24)
 - OR (감염수/연구) = 1.10 (0.81 - 1.50)
 - 감염률 = 0.89 (0.78 - 1.03)

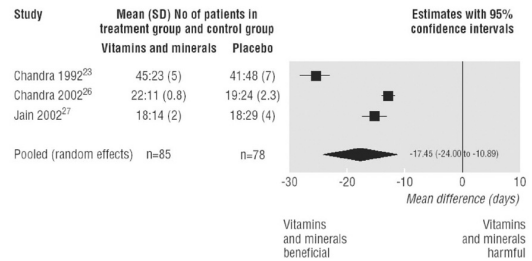
| Study (location) | Age of trial participants in years | Duration of follow-up | Infections assessed | No of subjects in placebo group | No of subjects in treatment group | Adjusted score | Comments |
|---|------------------------------------|-----------------------|--|---|---|----------------|--|
| Cheney et al 1980 (France) ¹⁰ | 65+ | 4 months | Respiratory, run, throat, ear, nose, mouth, urinary and gynaecological infections | 168 (of which 7 were lost to follow-up; sample size of 161) | 110 (of which 7 were lost to follow-up; leaving an effective sample size of 103) | 3 | Double blind |
| Gordon et al 1990 (France) ¹¹ | 65+ | 2 years | Respiratory and symptomatic otomycological infections | 182 (of which a withdrawal and 51 died during the study, but all were included in analysis) | 181 (of which 3 withdrew and 51 died during the study, but all were included in analysis) | 4 | A double blind, 2-2 factorial trial comparing placebo and nifedipine only included 70 patients who were included in the analysis Excluded from this analysis |
| Chander 1992 (United States) ¹² | 65+ | 12 months | Any infection (diagnosis was based on clinical features and laboratory tests included blood count, radiography of the chest and sputum, bacterial and fungal culture of sputum, urine and blood, C reactive protein, and erythrocyte sedimentation rate) | 48 | 48 | 4 | Double blind |
| Barringer et al 2000 (United States) ¹³ | 65+ | 12 months | Upper respiratory tract infection, lower respiratory tract infection, influenza like syndrome, gastroenteroviral infection, and urinary tract infection | 17 | 18 (65 (2 dropped out and were lost to follow-up leaving an effective sample size of 16)) | 4 | Prospect aged 65 years were excluded from the study A large proportion of subjects had excluded double blind |
| Grant et al 2002, (Netherlands) ¹⁴ | 65+ | 15 months (mean) | Acute respiratory tract infection | 230 | 240 | 3 | A double blind, 2-2 factorial trial comparing placebo and nifedipine + multivitamin + vitamin C. 15 only and multivitamin + vitamin C were excluded from meta-analysis |
| Chander 2002 (Question not specified) ¹⁵ | 50-65 | 12 months | Common cold infection. Diseases diagnosed by fever, cough, elevated erythrocyte sedimentation rate and C reactive protein, a mix of the strains and chest, blood cultures, sputum culture, and urine culture | 22 (three lost to follow-up, leaving an effective sample size of 19) | 22 | 4 | Double blind |
| Jay 2002 (India) ¹⁶ | 51-78 | 12 months | Respiratory infections | 18 | 18 | 3 | Blinding unclear |
| Gordon et al 1997 (France) ¹⁷ | 65+ | 2 years | Respiratory and symptomatic otomycological infections | 23 (of which 7 dropped out before and lost were included in analysis) | 21 (of which 7 dropped out before and lost were included in analysis) | 4 | A double blind, 2-2 factorial trial comparing placebo and nifedipine only included 70 patients who were included in the analysis Excluded from this analysis |

[illegible]

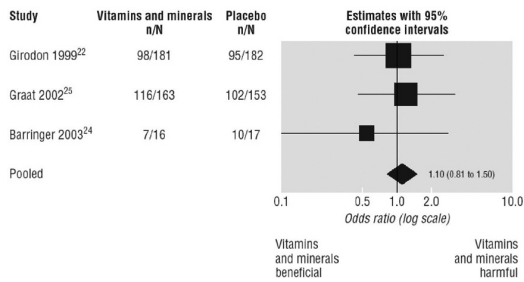
Table 3 Reporting of infections by different definition of outcome (binary)

| Study (location) | Mean days of infection | At least one infection | Infection rate |
|---|------------------------|------------------------|----------------|
| Chavance et al 1993 (France) ²¹ | | | X |
| Girodon et al 1999 (France) ²² | | X | |
| Chandra 1992 (United States) ²³ | X | | |
| Barringer et al 2003 (United States) ²⁴ | | X | |
| Graat et al 2002 (Netherlands) ²⁵ | | X | X |
| Chandra 2002 (location not specified) ²⁶ | X | | |
| Jain 2002 (India) ²⁷ | X | | X |
| Girodon et al 1997 (France) ²⁸ | | | X |
| Total instances reported | 3 | 3 | 4 |

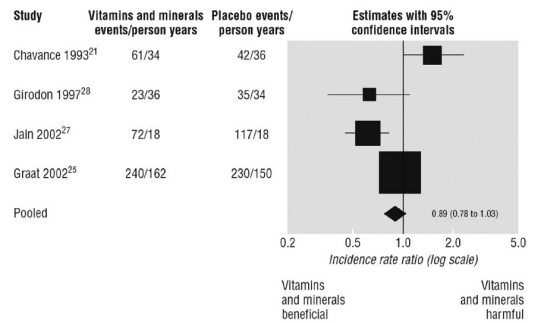
Number of Days of Infection



OR for at least One Infection during the Study Periods



Incidence Rate Ratio for Infection



Effect of an Enriched Drink on Cognitive Function in Frail Elderly Persons

Wendeline Wouters-Wesseling,¹ Lisette W. Wagenaar,¹ Marja Rozendaal,¹ Jan Berend Deijen,² Lisette C. de Groot,³ Jacques G. Bindels,^{1,3} and Wija A. van Staveren³

- 101 frail adults >65세
- BMI < 25
- Enriched drink for 6 months
- Cognitive Function
 - Cartegory Fluency(CF), Word Learning Test(WLT)
 - Recognition Memory Test for Words
- Results
 - 67명이 완성
 - CF professions, WLT에서 유의한 차이

Table 1. Composition of the Dietary Supplement per Daily Dose (250 ml)

| Nutrient | Amount |
|-----------------------|--------------------|
| Energy (MJ) (kcal) | 1.05 (250) |
| Protein (whey) (g) | 8.75 (14% energy) |
| Carbohydrates (g) | 28.5 (46% energy) |
| Fat (g) | 11.25 (40% energy) |
| Dietary fiber (g) | 4.5 |
| Sodium (mg) | 80 |
| Potassium (mg) | 550 |
| Chloride (mg) | 40 |
| Calcium (mg) | 400 |
| Phosphorus (mg) | 400 |
| Magnesium (mg) | 100 |
| Iron (mg) | 9 |
| Zinc (mg) | 18 |
| Copper (mg) | 3 |
| Manganese (mg) | 4 |
| Fluoride (µg) | 75 |
| Molybdenum (µg) | 40 |
| Selenium (µg) | 85 |
| Chromium (µg) | 35 |
| Iodine (µg) | 150 |
| Vitamin A (µg) | 240 |
| Carotenoids (µg) | 3 |
| Vitamin D (µg) | 13 |
| Vitamin E (mg) | 70 |
| Vitamin K (µg) | 80 |
| Vitamin C (mg) | 250 |
| Vitamin B1 (mg) | 1.9 |
| Vitamin B2 (mg) | 1.9 |
| Vitamin B6 (mg) | 2.5 |
| Vitamin B12 (µg) | 5.3 |
| Niacin (mg NE) | 14 |
| Pantothenic acid (mg) | 4.5 |
| Folate (µg) | 480 |
| Biotin (µg) | 70 |
| Coenzyme Q10 (mg) | 3 |
| Flavonoids (mg) | 19 |

Table 3. Mean Scores on Memory Tests at Baseline and Changes After 6 Months of Nutritional Supplementation in Frail Elderly Persons Receiving Placebo (n = 33) or Supplement (n = 34)

| Test | Baseline (Mean \pm SD) | | Change (Mean \pm SEM) | | p | 95% CI |
|---|--------------------------|----------------|-------------------------|----------------|-------|--------|
| | Placebo | Supplement | Placebo | Supplement | | |
| Neuropsychological tests | | | | | | |
| WLT | 6.1 \pm 2.2 | 4.4 \pm 2.1* | -0.1 \pm 0.3 | 0.9 \pm 0.3 | 0.014 | -1.71 |
| WLT delayed ^d | 6.6 \pm 2.1 | 4.7 \pm 2.8* | 0.3 \pm 0.4 | 0.9 \pm 0.4 | 0.152 | -1.85 |
| RMTW ^e | 40.9 \pm 5.5 | 40.3 \pm 4.9 | 0.7 \pm 1.2 | -1.1 \pm 0.9 | 0.383 | -1.19 |
| Category fluency animals | 15.2 \pm 4.3 | 13.9 \pm 4.5 | 0.9 \pm 0.7 | 0.9 \pm 0.6 | 0.473 | -1.88 |
| Category fluency professions | 11.9 \pm 3.4 | 10.1 \pm 4.3 | -0.6 \pm 0.5 | 1.2 \pm 0.7 | 0.017 | -3.46 |
| Biochemistry | | | | | | |
| Plasma homocysteine (μ mol/L) ^f | 17.6 \pm 5.0 | 18.4 \pm 7.9 | -0.3 \pm 2.9 | -6.3 \pm 5.9 | 0.000 | — |
| Plasma vitamin B12 (pmol/L) ^g | 290 \pm 99 | 304 \pm 118 | -8 \pm 16 | 105 \pm 50 | 0.003 | — |

Notes: * p < .01 versus placebo.

^a n = 27 for both groups.^b n = 30 for placebo; n = 28 for supplement.^c n = 23 for placebo; n = 2 for supplement, nonparametric test.^d n = 14 for placebo; n = 12 for supplement, nonparametric test.

WLT = Word learning test; RMTW = recognition memory test for words.

강의 내용

- Homocystein related Vitamin B complex
- Vitamin D
 - With Calcium
- Multivitamin
- Antioxidant (Vitamin)
- Phytochemical

4. Antioxidants

- Aging Mechanism 관련
 - Mitochondria
- Dementia시 Amyloid- β protein 침착
 - Oxidative Stress 증가
 - 결과인지 원인인지 알 수 없음
- Vit C, E, Carotenoids
 - 야채 섭취 높은 군이 CVA 적다
 - Vit E 2000 IU – institutionalization 더 늦음
- 전반적으로는 Conflicting Results

ORIGINAL CONTRIBUTION

Reduced Risk of Alzheimer Disease in Users of Antioxidant Vitamin Supplements

The Cache County Study

Peter P. Zandi, PhD; James C. Anthony, PhD; Ara S. Khachaturian, PhD; Stephanie V. Stone, PhD; Deborah Gustafson, PhD; JoAnn T. Tschann, PhD; Maria C. Norton, PhD; Kathleen A. Welsh-Bohmer, PhD; John C. S. Breiner, MD; for the Cache County Study Group

Background: Antioxidants may protect the aging brain against oxidative damage associated with pathological changes of Alzheimer disease (AD).

Objective: To examine the relationship between antioxidant supplement use and risk of AD.

Design: Cross-sectional and prospective study of dementia. Elderly (65 years or older) county residents were assessed in 1995 to 1997 for prevalent dementia and AD, and again in 1998 to 2000 for incident illness. Supplement use was ascertained at the first contact.

Setting: Cache County, Utah.

Participants: Among 4740 respondents (93%) with data sufficient to determine cognitive status at the initial assessment, we identified 200 prevalent cases of AD. Among 3227 survivors at risk, we identified 104 incident AD cases at follow-up.

Main Outcome Measure: Diagnosis of AD by means of multistage assessment procedures.

Results: Analyses of prevalent and incident AD yielded similar results. Use of vitamin E and C (ascorbic acid) supplements in combination was associated with reduced AD prevalence (adjusted odds ratio, 0.22; 95% confidence interval, 0.05-0.60) and incidence (adjusted hazard ratio, 0.36; 95% confidence interval, 0.09-0.90). A trend toward lower AD risk was also evident in users of vitamin E and multivitamins containing vitamin C, but we saw no evidence of a protective effect with use of vitamin E or vitamin C supplements alone, with multivitamins alone, or with vitamin B-complex supplements.

Conclusions: Use of vitamin E and vitamin C supplements in combination is associated with reduced prevalence and incidence of AD. Antioxidant supplements merit further study as agents for the primary prevention of AD.

Arch Neurol. 2004;61:82-88

Vitamin Supplement and Prevalent AD

(Zandi et al. 2004. Arch Neur)

- Vit E > 400 IU
- Vit C > 500mg

| | No. With AD/Total No.* | Unadjusted OR (95% CI) | Adjusted OR† (95% CI) |
|---|------------------------|------------------------|-----------------------|
| Any vitamin E | | | |
| No | 186/4127 | 1.0 | 1.0 |
| Yes | 8/482 | 0.35 (0.15-0.67) | 0.44 (0.19-0.95) |
| Any vitamin C (ascorbic acid) | | | |
| No | 175/3951 | 1.0 | 1.0 |
| Yes | 10/658 | 0.63 (0.38-0.99) | 0.80 (0.46-1.30) |
| Any multivitamins | | | |
| No | 152/3219 | 1.0 | 1.0 |
| Yes | 42/1400 | 0.62 (0.44-0.88) | 0.63 (0.43-0.92) |
| Any B-complex vitamins | | | |
| No | 188/4430 | 1.0 | 1.0 |
| Yes | 6/189 | 0.74 (0.29-1.95) | 1.05 (0.39-2.35) |
| Supplements in combination | | | |
| No vitamin E, C, or multivitamins | 138/2928 | 1.0 | 1.0 |
| Multivitamins, no vitamin E or C | 32/87 | 0.67 (0.44-0.97) | 0.60 (0.39-0.91) |
| Vitamin C, no vitamin E or multivitamins | 9/46 | 1.28 (0.60-2.43) | 1.47 (0.63-3.08) |
| Vitamin E, no vitamin C or multivitamins | 4/73 | 1.13 (0.34-2.78) | 1.15 (0.32-3.21) |
| Vitamin C and multivitamins, no vitamin E | 7/186 | 0.76 (0.32-1.54) | 0.99 (0.39-2.15) |
| Vitamin E and multivitamins, no vitamin C | 1/83 | 0.24 (0.01-1.08) | 0.34 (0.02-1.54) |
| Vitamin E and C‡ | 3/336 | 0.18 (0.04-0.47) | 0.22 (0.05-0.93) |

Vitamin Supplement and Incident AD

; Cache County Study

(Zandi et al. 2004. Arch Neur)

| | No. With AD/Total Person-Years* | Unadjusted HR (95% CI) | Adjusted HR† (95% CI) |
|---|---------------------------------|------------------------|-----------------------|
| Any vitamin E | | | |
| No | 93/8778 | 1.0 | 1.0 |
| Yes | 6/1172 | 0.48 (0.19-1.02) | 0.53 (0.20-1.12) |
| Any vitamin C (ascorbic acid) | | | |
| No | 88/8411 | 1.0 | 1.0 |
| Yes | 11/1539 | 0.68 (0.34-1.23) | 0.74 (0.37-1.35) |
| Any multivitamins | | | |
| No | 70/6818 | 1.0 | 1.0 |
| Yes | 28/5132 | 0.90 (0.58-1.38) | 0.79 (0.50-1.22) |
| Any B-complex vitamins | | | |
| No | 95/9490 | 1.0 | 1.0 |
| Yes | 4/460 | 0.87 (0.27-2.09) | 0.94 (0.28-2.29) |
| Supplements in combination | | | |
| No vitamin E or C or multivitamins | 64/5928 | 1.0 | 1.0 |
| Multivitamins, no vitamin E or C | 21/2127 | 0.91 (0.55-1.47) | 0.77 (0.45-1.27) |
| Vitamin C, no vitamin E or multivitamins | 3/312 | 0.89 (0.22-2.42) | 1.25 (0.30-3.52) |
| Vitamin E, no vitamin C or multivitamins | 2/159 | 1.17 (0.19-3.77) | 1.20 (0.19-4.13) |
| Vitamin C and multivitamins, no vitamin E | 5/411 | 1.13 (0.39-2.55) | 0.94 (0.32-2.20) |
| Vitamin E and multivitamins, no vitamin C | 1/197 | 0.47 (0.03-2.14) | 0.47 (0.03-2.22) |
| Vitamin E and C‡ | 3/316 | 0.34 (0.06-0.92) | 0.35 (0.03-0.93) |

Different Forms of Vitamin E

- 4종 Tocopherol + 4종 Tocotrienol
 - α, β, γ, δ
 - α-tocopherol; 인체 활성화 형태
 - Natural form : RRR-AT
 - α TTP에 훨씬 친화적임
 - Synthetic form : all-rac-AT
 - RRR-AT > 800 IU + Vit C regimen

Table 1. Summary of studies relating antioxidant intake and risk of AD

| Reference | Setting | Design | Participants | Exposure | Outcome | Results |
|--------------------------------|--|--------|--|--|---|--|
| Masaki et al ¹⁰ | Honolulu-Age Cohort | Cohort | 3985 men, age 71-93 years | Use of supplements of vitamins C and E | AD, mixed dementia, vascular dementia, Cognitive function | Intake of supplements of both vitamins related to low risk of vascular dementia but not related to risk of AD; intake of either related to better cognitive function |
| Grodstein et al ¹¹ | Nurses' Health Study | Cohort | 14 958 women, age 70-79 years | Use of supplements containing vitamins C and E | TICS, delayed recall of TICS ten-word list, delayed recall of EBMT, verbal fluency, digit span backwards test | Current users of supplements had better global scores than non-users |
| Zandi et al ¹² | Catch County Cohort Study | Cohort | 4540, 90% age ≥65 years | Use of vitamin C and E supplements | Incident AD | Reduction in risk of AD in users of combination of vitamin C and E supplements, but not in users of these supplements alone |
| Engelhart et al ¹³ | Rotterdam Study | Cohort | 5395, age ≥65 years | Intake of vitamins C and E, carotenes, and flavonoids measured by SFFQ | | Dietary vitamins C and E inversely related to risk of dementia |
| Morris et al ¹⁴ | Chicago Health and Aging Project | Cohort | 2889 community residents, age 65-102 years | Intakes of vitamins E and C and carotenes from food | Cognitive change of EBMT, MMSE, symbol digit modalities test (baseline and 3 years) | Vitamin E is inversely related to cognitive decline |
| Morris et al ¹⁵ | Chicago Health and Aging Project | Cohort | 815 community dwelling people age ≥65 years | Intake of dietary and supplement vitamins C and E, and β carotene measured by SFFQ | Incident AD | Dietary vitamin E intake inversely related with lower risk of AD. No association for intake of vitamin E supplement, vitamin C, or carotenes |
| Luchsinger et al ¹⁶ | Washington Height Columbia Aging Project | Cohort | 960 community dwelling individuals age ≥65 years | Intake of dietary and supplement vitamins C and E and carotenes measured by SFFQ | Incident AD | No relation between antioxidants with AD |

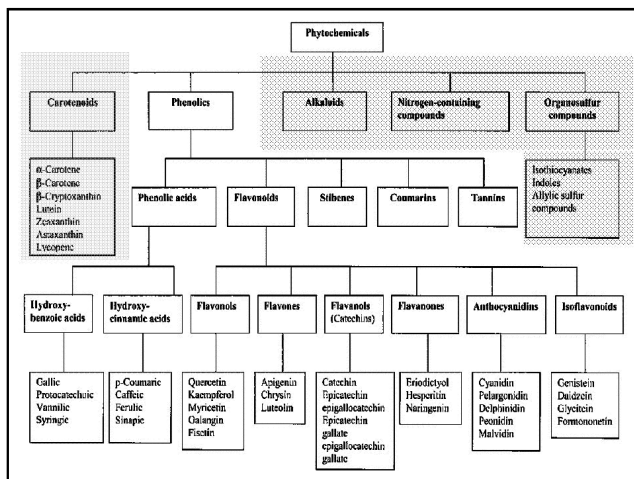
TICS=telephone interview of cognitive status; EBMT=East Boston Memory Test; SFFQ=semi-quantitative food frequency questionnaire.

강의 내용

- Homocystein related Vitamin B complex
- Vitamin D
 - With Calcium
- Multivitamin
- Antioxidant (Vitamin)
- Phytochemical

5. 'Phyto-chemical'

- **Phyto-**
 - Greek word for 'plants'
- **Bioactive non-nutrient plant compound**
 - may help prevent diseases like cancer and heart disease
 - *Anti-oxidant effect*, Metabolic effect
- **Phyto-nutrient**
 - 5대 영양소의 포함 여부
- 5,000종류 이상이 알려짐
 - 계속 증가하고 있음



건강 식이 ≡ 과일, 야채

■ Swedish Mammography Screening Cohort

(Int J Epidemiol 2002;31(4))

- 건강식이 : 야채, 과일, 생선, 견과류, 저지방우유, 요구르트, 복합 당류

- 비건강식이: 고기, 정제된 탄수화물, 설탕, 포화지방음식

→ 한달 16회 이상의 건강 식이군이, 8회 미만을 섭취한 군에 비해 총사망위험 46% 감소

건강식 횟수가 1회 증가할수록 총 사망위험 5% 감소

건강식 및 비건강식 횟수에 따른 사망비교

| | 건강식 횟수 한달 16회이상 vs 8회이하 | 비건강식 횟수 한달 16회이상 vs 8회이하 |
|---------|----------------------------|-----------------------------|
| 암사망 | 0.76(0.60-0.96) | 1.52(1.13-2.05) |
| 심장질환사망 | 0.47(0.33-0.68) | 0.79(0.47-1.32) |
| 뇌혈관질환사망 | 0.40(0.22-0.73) | 0.96(0.47-1.97) |

(Int J Epidemiol 2002;31(4))

Phytochemical의 역할

- 항 산화 작용
- 항 암 작용
- 항 혈전 작용
- 혈당, 혈압 조절 작용
- 항 동맥경화 작용
- 면역 증강 기능

1) Anti-thrombotic Action

- 3 'G'
- Garlic
- Gingerol (Ginger)
- Ginkgo
- Others
- Wine, Grape juice, Isoflavone, Carnosol
- 기전
- COX, Lipoxygenase modulation

2) 혈당, 혈압 조절 작용

- Insulin like activity
- Myricetin
- Starch enzyme 저하제
- Tannin, Phytic acid
- 혈압 저하
- Flavonoids, Garlic

3) 항 동맥 경화

- 항 콜레스테롤
- Phytosterins; plant steroids
- Garlic
- 항 동맥 경화
- Soy

The American Journal of CLINICAL NUTRITION

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Institution: Seoul Natl Univ Col of Med Lib Sign In as Member and Individual (Non-member)

American Journal of Clinical Nutrition, Vol. 76, No. 3, 560-568, September 2002

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Original Research Communication

Flavonoid intake and risk of chronic diseases^{1,2}

- Finnish Mobile Clinic Health Examination Survey
- 1966 – 1972,
- 10,054 men and women
- Results
 - Quercetin
 - IHD, Lung Ca, Asthma, DM
 - Myricetin
 - Prostate Ca, DM
 - CVD
 - Kaempferol, Naringenin, Hesperetin.
 - Asthma
 - Quercetin, Naringenin, Hesperetin

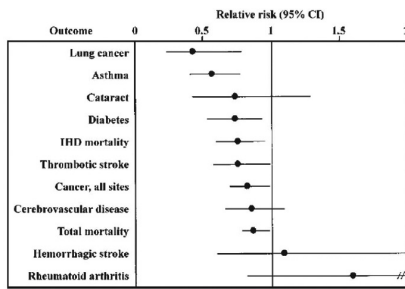


FIGURE 1. Relative risks (●) and 95% CIs (horizontal bars) of chronic diseases between the highest (>47 g/d) and lowest (0 g/d) quartiles of apple intake. The relative risks were adjusted for sex, age, disease-specific nondietary confounding factors, and intakes of vegetables and fruit other than apples. IHD, ischemic heart disease.

ORIGINAL RESEARCH COMMUNICATION

Flavonoid intake and the risk of cardiovascular disease in women^{1,2,3}

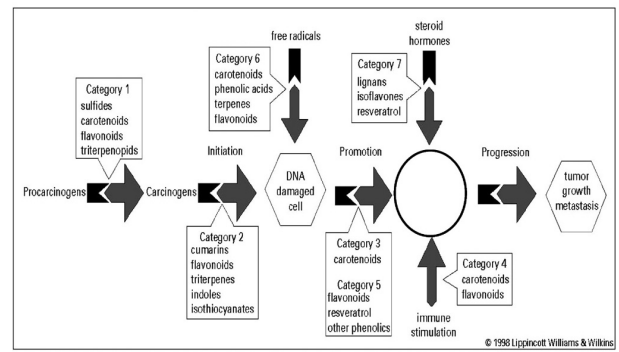
Howard D Sesso, J Michael Gaziano, Simin Liu and Julie E Buring

¹ From the Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School.

- The Women's Health Study
- **39,876** female US health professionals
- 6.9 yr FU
- Results
- Not significant

| | Category of intake ² | | | | P for trend |
|---|---------------------------------|-------------------|-------------------|-------------------|-------------|
| | 1st (Lowest) | 2nd | 3rd | 4th (Highest) | |
| Tea | | | | | |
| No. of women | 12383 | None | 15862 | 8472 | 1185 |
| No. of CVD cases | 240 | 303 | 162 | 17 | |
| Age- and treatment-adjusted RR ¹ | 1.00 (ref) | 1.05 (0.88, 1.24) | 1.06 (0.87, 1.30) | 0.85 (0.52, 1.40) | 0.54 |
| Multivariate-adjusted RR ⁴ | 1.00 (ref) | 1.14 (0.95, 1.36) | 1.15 (0.93, 1.42) | 0.74 (0.44, 1.25) | 0.36 |
| No. of important vascular events | 178 | 205 | 126 | 6 | |
| Age- and treatment-adjusted RR ¹ | 1.00 (ref) | 0.95 (0.78, 1.16) | 1.12 (0.89, 1.40) | 0.41 (0.18, 0.92) | 0.16 |
| Multivariate-adjusted RR ⁴ | 1.00 (ref) | 1.02 (0.83, 1.26) | 1.13 (0.93, 1.51) | 0.33 (0.14, 0.80) | 0.07 |
| Broccoli | | | | | |
| No. of women | 2173 | 23201 | 10960 | 1900 | |
| No. of CVD cases | 67 | 444 | 183 | 32 | |
| Age- and treatment-adjusted RR ¹ | 1.00 (ref) | 0.65 (0.51, 0.85) | 0.59 (0.45, 0.79) | 0.58 (0.38, 0.89) | 0.027 |
| Multivariate-adjusted RR ⁴ | 1.00 (ref) | 0.75 (0.57, 0.99) | 0.70 (0.51, 0.96) | 0.71 (0.44, 1.15) | 0.21 |
| No. of important vascular events | 49 | 307 | 131 | 23 | |
| Age- and treatment-adjusted RR ¹ | 1.00 (ref) | 0.62 (0.46, 0.84) | 0.61 (0.44, 0.85) | 0.58 (0.35, 0.95) | 0.11 |
| Multivariate-adjusted RR ⁴ | 1.00 (ref) | 0.73 (0.53, 1.01) | 0.73 (0.51, 1.06) | 0.72 (0.41, 1.27) | 0.56 |
| Apples | | | | | |
| No. of women | 3557 | None | 17697 | 13670 | 3130 |
| No. of CVD cases | 90 | 323 | 245 | 52 | |
| Age- and treatment-adjusted RR ¹ | 1.00 (ref) | 0.73 (0.57, 0.97) | 0.68 (0.53, 0.96) | 0.58 (0.41, 0.81) | 0.015 |
| Multivariate-adjusted RR ⁴ | 1.00 (ref) | 0.82 (0.64, 1.04) | 0.87 (0.66, 1.14) | 0.78 (0.52, 1.10) | 0.74 |
| No. of important vascular events | 63 | 228 | 182 | 31 | |
| Age- and treatment-adjusted RR ¹ | 1.00 (ref) | 0.73 (0.55, 0.97) | 0.72 (0.54, 0.96) | 0.49 (0.32, 0.76) | 0.015 |
| Multivariate-adjusted RR ⁴ | 1.00 (ref) | 0.83 (0.62, 1.11) | 0.86 (0.69, 1.32) | 0.66 (0.40, 1.08) | 0.56 |
| Onions | | | | | |
| No. of women | 16309 | None | 16029 | 3722 | 1978 |
| No. of CVD cases | 291 | 311 | 78 | 39 | |
| Age- and treatment-adjusted RR ¹ | 1.00 (ref) | 1.03 (0.88, 1.21) | 1.08 (0.84, 1.39) | 1.03 (0.73, 1.44) | 0.73 |
| Multivariate-adjusted RR ⁴ | 1.00 (ref) | 1.00 (0.85, 1.19) | 1.18 (0.91, 1.54) | 1.00 (0.68, 1.46) | 0.50 |
| No. of important vascular events | 203 | 227 | 55 | 30 | |
| Age- and treatment-adjusted RR ¹ | 1.00 (ref) | 1.10 (0.91, 1.33) | 1.11 (0.82, 1.51) | 1.17 (0.79, 1.72) | 0.43 |
| Multivariate-adjusted RR ⁴ | 1.00 (ref) | 1.04 (0.85, 1.28) | 1.21 (0.89, 1.66) | 1.15 (0.75, 1.78) | 0.23 |
| Tofu | | | | | |
| No. of women | 34756 | None | 2142 | 1058 | |
| No. of CVD cases | 655 | 35 | 23 | | |
| Age- and treatment-adjusted RR ¹ | 1.00 (ref) | 0.89 (0.64, 1.25) | 1.18 (0.78, 1.79) | | 0.76 |
| Multivariate-adjusted RR ⁴ | 1.00 (ref) | 1.06 (0.77, 1.55) | 1.17 (0.71, 1.91) | | 0.45 |
| No. of important vascular events | 467 | 24 | 16 | | |
| Age- and treatment-adjusted RR ¹ | 1.00 (ref) | 0.86 (0.57, 1.29) | 1.15 (0.70, 1.89) | | 0.95 |
| Multivariate-adjusted RR ⁴ | 1.00 (ref) | 1.03 (0.67, 1.57) | 1.16 (0.65, 2.08) | | 0.64 |

4) Anti-carcinogenesis Effects



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Volume 14(2) April 2005 pp 139-142

Resveratrol and breast cancer risk
[Research papers: Breast Cancer]

Levi, F^{1,2}, Pasche, C², Luchini, F¹, Ghidoni, R², Ferraroni, M², La Vecchia, C^{1,3}

- Resveratrol
 - French Paradox
 - Grape Skin(숙성되면서 증가), Mulberry, Peanut
- Case-Control Study
 - Case : 369
 - Control : 602
- Results
 - Odds Ratio
 - Intermediate : 0.5
 - The highest : 0.39
 - Significant only for 'Grape'

Odds Ratios for Breast Cancer

Table 1 Distribution of 369 cases of breast cancer and 602 controls according to various sources of dietary resveratrol intake, and corresponding odds ratios (OR) and 95% confidence intervals (CI). Vaud, Switzerland, 1993-2003

| | 1st tertile ^a | | 2nd tertile | | 3rd tertile | | χ^2 , trend |
|-----------------------|--------------------------|--------------------------|---------------|------------------|---------------|------------------|------------------|
| | Case/controls | OR ^b (95% CI) | Case/controls | OR (95% CI) | Case/controls | OR (95% CI) | |
| Total (wine & grapes) | 138:208 | 1.0 | 84:191 | 0.53 (0.34-0.72) | 182:203 | 0.39 (0.28-0.52) | 18.80 (P<0.001) |
| Wine, total | 184:408 | 1.0 | 89:92 | 1.05 (0.18-6.25) | 116:104 | 1.80 (0.28-9.28) | 1.95 (P = 0.25) |
| Grapes | 188:213 | 1.0 | 79:151 | 0.84 (0.44-0.93) | 122:238 | 0.55 (0.39-0.76) | 12.79 (P<0.001) |

^aReference category: tertile of total resveratrol determined on controls distribution. The upper cut-points for the tertile of total resveratrol intake (μg/day) ranged between 0.0 and 78.0 for the 1st tertile (lowest), 73.1 and 180.7 for the 2nd tertile, >180.7 for the 3rd tertile (highest); intake from wine was 0.0 for the 1st tertile, ranged between 0.1 and 176.8 for the 2nd tertile, >176.8 for the 3rd tertile; intake from grapes ranged between 0.0 and 72.2 for the 1st tertile, 72.9 and 128.4 for the 2nd tertile, >128.4 for the 3rd tertile.

^bOR adjusted for age, education, body mass index, hormone replacement therapy, menopausal status, parity, energy intake, and total alcohol consumption.

Odds Ratios for Breast Cancer in strata of various covariates

| | 2nd tertile ^a OR ^b (95% CI) | 3rd tertile OR (95% CI) | μ^2 , trend |
|-------------------------|--|----------------------------|-----------------------|
| Age at menopause | | | |
| Pre-peri | 0.58 (0.29–1.16) | 0.46 (0.20–1.05) | 3.72 ($P = 0.054$) |
| < 50 years | 0.42 (0.21–0.87) | 0.38 (0.15–0.91) | 5.88 ($P = 0.015$) |
| ≥ 50 years | 0.46 (0.24–0.86) | 0.41 (0.18–0.93) | 6.32 ($P = 0.012$) |
| Parity | | | |
| 0 | 0.45 (0.20–1.04) | 0.29 (0.10–0.86) | 5.50 ($P = 0.019$) |
| ≥ 1 | 0.51 (0.33–0.78) | 0.40 (0.24–0.68) | 13.77 ($P = 0.000$) |
| HRT | | | |
| Never | 0.52 (0.34–0.81) | 0.46 (0.27–0.77) | 10.65 ($P = 0.01$) |
| Ever | 0.26 (0.11–0.61) | 0.16 (0.05–0.52) | 11.85 ($P = 0.001$) |
| BMI (kg/m) ² | | | |
| < 25 | 0.52 (0.31–0.87) | 0.37 (0.18–0.73) | 9.84 ($P = 0.02$) |
| ≥ 25 | 0.41 (0.23–0.73) | 0.40 (0.21–0.77) | 8.80 ($P = 0.003$) |

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REPORTS

Intake of Flavonoids and Lung Cancer

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- 582 Lung Ca Case vs. 582 Control
- 242 Food Item
- CYP1A1*2
- Results
 - Quercetin(사과, 양파), Naringin(자몽)은 유의하게 Lung Ca OR 감소
 - CYP1A1 genotype Inhibition

Table 2. Odds ratios* (95% confidence intervals) for lung cancer by quantile

| | Odds ratio (95% confidence interval) by | | | | Two-sided <i>P</i> for trend† |
|---|---|----------------|----------------|-----------------------|----------------------------------|
| | Q ₁ (low) | Q ₂ | Q ₃ | Q ₄ (high) | |
| A) Intake of flavonoid-rich foods‡ | | | | | |
| Onions | 1.0 (referent) | 1.4 (0.9–2.3) | 0.9 (0.5–1.4) | 0.5 (0.3–0.9) | .001 |
| Broccoli | 1.0 (referent) | 1.0 (0.6–1.6) | 0.8 (0.5–1.3) | 0.9 (0.5–1.4) | .48 |
| Celery | 1.0 (referent) | 0.7 (0.4–1.1) | 0.8 (0.5–1.4) | 0.8 (0.5–1.3) | .70 |
| Soy products | 1.0 (referent) | 1.6 (1.0–2.7) | 1.2 (0.7–2.2) | 1.0 (0.5–1.8) | .28 |
| Apples | 1.0 (referent) | 0.9 (0.6–1.4) | 1.0 (0.6–1.6) | 0.6 (0.4–1.0) | .03 |
| White grapefruit | 1.0 (referent) | 0.8 (0.4–1.6) | 0.5 (0.2–0.9) | | .02 |
| Pink grapefruit | 1.0 (referent) | 0.7 (0.5–1.2) | 0.9 (0.6–1.6) | | .91 |
| Other citrus fruits | 1.0 (referent) | 0.9 (0.5–1.4) | 0.9 (0.5–1.4) | 0.9 (0.5–1.4) | .74 |
| Red wine | 1.0 (referent) | 0.8 (0.4–1.8) | 0.7 (0.4–1.2) | | .20 |
| White wine | 1.0 (referent) | 0.8 (0.4–1.4) | 1.0 (0.6–1.7) | | .96 |
| Black tea | 1.0 (referent) | 1.5 (0.8–2.6) | 1.1 (0.7–1.8) | 1.1 (0.7–1.8) | .83 |
| Green tea | 1.0 (referent) | 1.0 (0.6–1.7) | 0.7 (0.4–1.3) | 0.9 (0.5–1.6) | .62 |
| B) Flavonoid intakes§ | | | | | |
| Quercetin | 1.0 (referent) | 0.9 (0.6–1.5) | 0.7 (0.4–1.1) | 0.7 (0.4–1.1) | .07 |
| Kaempferol | 1.0 (referent) | 1.1 (0.6–1.7) | 0.9 (0.6–1.5) | 0.9 (0.5–1.4) | .41 |
| Myricetin | 1.0 (referent) | 1.7 (1.0–2.7) | 1.5 (0.9–2.4) | 1.0 (0.6–1.6) | .42 |
| Hesperidin | 1.0 (referent) | 1.1 (0.7–1.8) | 1.2 (0.7–1.9) | 1.2 (0.7–2.0) | .54 |
| Naringin | 1.0 (referent) | 0.7 (0.4–1.2) | 0.7 (0.5–1.1) | | .17 |
| Total flavonoids | 1.0 (referent) | 0.8 (0.5–1.4) | 1.3 (0.8–2.1) | 0.8 (0.5–1.4) | .89 |

Table 3. Odds ratios* (95% confidence intervals) for lung cancer cell types by quantile of intake of onions, apples, white grapefruit, quercetin, and naringin

| Cell type† | Odds ratio (95% confidence interval) by | | | | Two-sided P for trend‡ |
|------------------|---|----------------|----------------|-----------------------|---------------------------|
| | Q ₁ (low) | Q ₂ | Q ₃ | Q ₄ (high) | |
| Onions | | | | | |
| SCC | 1.0 (referent) | 1.6 (0.4–5.6) | 0.7 (0.2–2.8) | 0.1 (0.0–0.6) | .003 |
| ADC | 1.0 (referent) | 1.0 (0.5–2.0) | 0.7 (0.4–1.5) | 0.6 (0.3–1.2) | .24 |
| Other | 1.0 (referent) | 1.0 (0.4–3.0) | 0.8 (0.3–2.2) | 0.3 (0.1–0.7) | .005 |
| Apples | | | | | |
| SCC | 1.0 (referent) | 0.6 (0.2–1.8) | 0.6 (0.2–1.9) | 0.5 (0.2–1.8) | .42 |
| ADC | 1.0 (referent) | 0.8 (0.4–1.5) | 1.2 (0.6–2.4) | 0.7 (0.3–1.3) | .23 |
| Other | 1.0 (referent) | 1.0 (0.5–2.1) | 0.5 (0.2–1.1) | 0.6 (0.3–1.4) | .26 |
| White grapefruit | | | | | |
| SCC | 1.0 (referent) | 0.2 (0.0–2.0) | 0.3 (0.1–1.6) | | .16 |
| ADC | 1.0 (referent) | 1.4 (0.6–3.5) | 0.6 (0.3–1.5) | | .39 |
| Other | 1.0 (referent) | 0.2 (0.0–1.2) | 0.3 (0.1–1.5) | | .09 |
| Quercetin | | | | | |
| SCC | 1.0 (referent) | 0.9 (0.3–3.1) | 1.6 (0.4–5.4) | 0.5 (0.2–1.9) | .44 |
| ADC | 1.0 (referent) | 1.2 (0.6–2.2) | 0.7 (0.4–1.4) | 0.9 (0.4–2.0) | .65 |
| Other | 1.0 (referent) | 0.8 (0.4–1.8) | 0.8 (0.4–1.7) | 0.5 (0.2–1.2) | .13 |
| Naringin | | | | | |
| SCC | 1.0 (referent) | 0.2 (0.1–1.1) | 0.2 (0.1–1.0) | | .06 |
| ADC | 1.0 (referent) | 0.9 (0.5–1.7) | 1.4 (0.7–2.5) | | .32 |
| Other | 1.0 (referent) | 0.7 (0.2–1.8) | 0.3 (0.1–0.9) | | .03 |

Table 4. Odds ratios* for lung squamous cell carcinoma by CYP1A1 genotype and onion intake

| Onion intake | CYP1A1 | n† | Odds ratio (95% confidence interval) |
|--------------|----------------|--------|--------------------------------------|
| ≤median | *1/*1 | 22/124 | 1.0 (referent) |
| >median | *1/*1 | 6/126 | 0.2 (0.1–0.5) |
| ≤median | *1/*2 or *2/*2 | 24/86 | 1.7 (0.7–4.0) |
| >median | *1/*2 or *2/*2 | 20/117 | 1.0 (0.4–2.4) |

Two-sided P for interaction‡ = .07

*Adjusted for age, sex, ethnicity, smoking status, duration, (duration)², number of cigarettes smoked per day, and β -carotene and saturated fat intakes.

†No. of case patients/No. of control subjects.

‡See "Statistical Methods" section for further details.

5) 항산화 작용

- 가장 활발히 연구되는 분야
- 대표적 작용 기전
 - Free radical quenching
 - LDL oxidation 저하
- Mixture 연구가 활발

강의 내용

- Homocystein related Vitamin B complex
- Vitamin D
 - With Calcium
- Multivitamin
- Antioxidant (Vitamin)
- Phytochemical