Dietary soy intake and changes of mammographic density in premenopausal Chinese women

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Research

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- Ms. Monique Chan

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Conflict of interest None
Prince of Wales Hospital
Chinese University of Hong Kong
# Breast cancer 2008

## World Age-Standardized Incidence Rate

<table>
<thead>
<tr>
<th>Region</th>
<th>ASR(W) per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>World</td>
<td>39.0</td>
</tr>
<tr>
<td>More developed regions</td>
<td>66.4</td>
</tr>
<tr>
<td>Less developed regions</td>
<td>27.3</td>
</tr>
<tr>
<td>South-Eastern Asia</td>
<td>31.0</td>
</tr>
</tbody>
</table>

Ferlay et al. Int J Cancer 2010
### Incidence and Mortality data
#### 2007

<table>
<thead>
<tr>
<th></th>
<th>New Case</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases registered</td>
<td>2,701</td>
<td>526</td>
</tr>
<tr>
<td>Rank</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Median age (years)</td>
<td>52</td>
<td>59</td>
</tr>
<tr>
<td>Crude Rate per 100,000</td>
<td>74.2</td>
<td>14.5</td>
</tr>
<tr>
<td>Age-standardized rate (World)*</td>
<td>52.7</td>
<td>10.0</td>
</tr>
<tr>
<td>Cumulative life-time risk (0-74 yrs)</td>
<td>1 in 20</td>
<td>1 in 102</td>
</tr>
<tr>
<td>Mortality : Incidence Ratio</td>
<td></td>
<td>0.20</td>
</tr>
</tbody>
</table>

Source: Hong Kong Cancer Registry Hospital Authority
Mammographic density and breast cancer risk

- Quantifiable measures of mammographically defined breast composition
- Substantial evidence on percent mammographic density a strong predictor of breast cancer risk
  - Maskarinec et al. AJE 2005
Factors influencing breast cancer risk

- Anthropometric
- Reproductive
- Lifestyle
  - Alcohol drinking
  - Smoking (active & passive)
  - Physical activity
  - Dietary
Soy foods

- Main source of isoflavones
- contain approx. 2-3.5 mg isoflavones per g soy protein
Soy isoflavones

A type of phytoestrogens

- Chemical structure similar to estrogen
  - estrogenic and anti-estrogenic

- Act as antioxidants
Soy foods

Other possible mechanisms

- Anticarcinogenic effect
- Stimulating sex hormone-binding globulin production
- Decrease the amount of free and active hormone in the blood
- Inhibiting angiogenesis

Source: Yamamoto et al. 2003
Controversy of soy

May have cancer-preventive effects when consumed early in life (during breast development)

- Shanghai Breast Cancer Study (Shu et al. 2001)
- Study of Asian-Americans (Wu et al. 2002)
- Migrant studies
Association of soy intake with mammographic pattern/density

- Highest Q vs lowest Q soy isoflavone intake related to lower risk of (tabar IV and V)
  
  OR = 0.44 (0.2-0.98)

- Highest quartile of soy intake related to lower PMD in Singapore postmenopausal women

  Wu A H et Cancer Epidemiolo Biomarkers Prev 2008; 17: 3358-3365

WCRF Study (2004-09)

Adolescent and adult soy intake and breast density in Chinese premenopausal women
Hypothesis

- To test the hypothesis that soy intake, in early and adult life reduces the likelihood of high-risk mammographic pattern or breast density in premenopausal women
Objectives

- To construct a population-based cohort of premenopausal women aged 35 to 46 years (N= 893)
- To study the association between soy food intake at different life stages, particularly adolescents, and high risk mammographic density
- To conduct longitudinal study to test the relation between soy food intake and changes of mammographic density
Sampling and recruitment

- A stratified cluster sampling method
- Samples were selected from three housing types in Shatin according to housing ratio:
  
  Public: Private: Homeownership (3:5:2)

- Strategies: active recruitment, mailing and media advertisements
- Overall response rate: 76.6%
Screening of participants

Inclusion criteria
- 35 – 45 y pre-menopausal Chinese women
- Stay in Hong Kong during the whole study (3 years)
- Have intact uterus and ovaries

Exclusion criteria
- History of benign breast diseases or any history of cancer; menopausal (incl. surgical); on long term antibiotics; on special diet such as high protein or diabetic meals
Data collection

Standardized measurements and questionnaire on potential confounding variables

- Height, weight, hip and waist circumference
- Sociodemographic, reproductive, physical activity, lifestyle factors
Data collection

- Validated soy food frequency questionnaire to assess current soy intake (T4)
- At baseline, life-history calendar assisted to assess intake of soy foods during
  - childhood (6 – 12 y) (T1)
  - adolescence (13 – 18 y) (T2)
  - young adulthood (20 – 34 y) (T3)
Mammographic pattern-density assessment

Mammograms made at baseline and 3-y followup

- cranio-caudal (CC)
- medio-lateral-oblique (MLO) views
Film digitizer

To digitize both sides of cranio-caudal views of mammogram films into images with DICOM format
Computer-assisted mammographic density assessment method

Cumulus4 program

- Developed at the University of Toronto
- To calculate percentage area of dense breast tissue from a digitalized film mammogram (CC view)
- Percent mammographic density
Demographic Features (n=817)

- Age: 40.9 ±2.95 (35 – 46 y)
- Marital status: about 80% married
- Employment status
  - About 50% full time job
  - 30% housewives
Demographics features

Place of birth
- Hong Kong: 74.3%

Educational level
- Tertiary education: 22.8%
- Completed secondary: 39.5%
- Some secondary: 27.3%
- Primary & below: 10.4%
Anthropometric measurements

- Body weight (kg) 56.5 ± 8.57
- BMI (kg/m²) 23.2 ± 3.33
- Waist circ (cm) 75.5 ± 8.1
Reproductive factors

- Age of menarche: $13.0 \pm 1.64$
- Age at first birth: $27.2 \pm 4.58$
- No. of live births: $1.85 \pm 0.74$
- Age of last pregnancy: $31.0 \pm 4.64$
- Breast feeding (mths): $6.04 \pm 8.73$
- Hormonal contraceptives use
  - Pills: 48.3%
  - Injection: 9.8%
Lifestyle Factors

- Current smokers: 4.3%
- Current drinker: 5.6%
  (≥1 – 2 times/week)
- Total physical activities score: 23.0 ± 2.81
Dietary Factors

- Energy intake (Kcal/day) 1673.5 ± 686.52
- Soy protein intake (g/day) 10.4 ± 9.99
- Isoflavone intake (mg/day) 22.3 ± 21.28
Percent mammographic density

Mean ± SD
38.8 ± 9.97
(0.0 – 73.1)
Regression analyses on baseline association of soy protein intake and PMD (adjusted)

<table>
<thead>
<tr>
<th>Soy protein intake (g/day)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 6-12y (T1)</td>
<td>0.040</td>
</tr>
<tr>
<td>Age 13-18y (T2)</td>
<td>0.042</td>
</tr>
<tr>
<td>Age 20-34 (T3)</td>
<td>0.215</td>
</tr>
<tr>
<td>Past year (T4)</td>
<td>0.753</td>
</tr>
<tr>
<td>Sum of intake (T1 and T2)</td>
<td>0.030</td>
</tr>
</tbody>
</table>

Adjusted for significant variables retained in stepwise multiple regression analyses (F-to-enter = <0.09, F-to-remove = ≥0.10): **waist circumference, body weight, number of live births, age of menarche and physical activity index**
### Joint effect of soy intake during early life and recent past year on PMD (highest quartile vs lower quartiles)

<table>
<thead>
<tr>
<th>Intake level</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower intake (Q1 to Q3) (T₁+T₂+T₃) and lower intake in T4</td>
<td>1.0</td>
</tr>
<tr>
<td>High intake (Q4) during T₁+T₂+T₃ and high intake in T4</td>
<td>0.46 (0.2-1.1)</td>
</tr>
</tbody>
</table>

Adjusted for age, BMI, WHR, physical activities, total energy intake
Q4 >13.84 g/d
Regression analyses on association of soy protein intake at different life stages and percent change of PMD over 3-year followup (adjusted)

<table>
<thead>
<tr>
<th>Soy protein intake (g/day)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 6-12y (T1)</td>
<td>0.246</td>
</tr>
<tr>
<td>Age 13-18y (T2)</td>
<td>0.109</td>
</tr>
<tr>
<td><strong>Age 20-34 (T3)</strong></td>
<td><strong>0.054</strong></td>
</tr>
<tr>
<td><strong>Current (T4)</strong></td>
<td><strong>0.020</strong></td>
</tr>
</tbody>
</table>

Adjusted for significant variables retained stepwise multiple regression analyses (F-to-enter = <0.09, F-to-remove = ≥0.10): baseline PMD, age of menarche, waist circumference
Limitations and strengths

- Population-based cohort
- Exposure assessment
  - Self-reported
  - Validated soy FFQ, use of food photos
  - Assisted with use of life history calendar
- Outcome evaluation
  - Single reader using highly reproductive computer assisted method, blinded to respondent characteristics
Summary

- Early life experience of soy food intake is associated with lower PMD in Chinese premenopausal women (35-45y)
- High current intake of soy and in young adulthood seems protective of high risk PMD changes over time
Further studies

- Cohort
- Longer followup of present cohort
- RCT on effect of soy intake on PMD
Implications

- If high life time soy intake during childhood, adolescent and adulthood protective of breast cancer risk (by lowering the percent mammographic breast density)

- Strategies to maximize the benefits of dietary soy intake in reduction of breast cancer risk
Thank you