

論文の内容の要旨

論文題目 Rice intake and colorectal cancer in Japanese men and women: the Japan Public Health Center-based prospective Study (JPHC Study)

(多目的コホート研究による日本人男女における米飯摂取と大腸がんの関連に関する研究)

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Introduction

Colorectal cancer is one of the most common cancers globally. The geographic variation greatly varies with high rates found in Australia and Western Europe and low rates in Africa and South-Central Asia. Environmental factors may contribute to colorectal cancer incidence. Some researchers speculate that the recent high colorectal cancer rates in Japan and Korea may partially be explained by a genetic predisposition. Alternatively, rice intake may be a surrogate of a traditional Japanese diet and thus may represent specific dietary patterns associated with colorectal cancer risk.

In Japan, a contradictory pattern exists. Rice may be inversely associated with colorectal cancer suggested by a trend of decreasing rice intake in Japan along with increasing colorectal cancer incidence rates. On the other hand, high colorectal cancer mortality rates in prefectures where large amounts of rice are consumed may imply a positive association. The association between rice and diabetes has been established, as has the association between diabetes and colorectal cancer. The association between the glycemic index and load and colorectal cancer has received more attention. Therefore, the main aim of this study was to:

- (1) Assess colorectal cancer risk by quartile of rice, bread, noodle, and cereal intake
- (2) Evaluate effect modification of main risk factors and rice on colorectal cancer
- (3) Compare risk differences by colorectal cancer subsite and gender

Data and Methods

The Japan Public Health Center-based prospective Study (JPHC Study) is an on-going cohort study focusing on cancer, cardiovascular and other lifestyle-related diseases, Approximately 140,000 Japanese citizens in 11 public health centers (PHC) throughout

Japan were recruited. At baseline (1990-1994) participants aged 40–69 years. In the present study the 5-year follow-up questionnaire was used as the starting point. The Tokyo PHC was excluded because no cancer incidence information was available, leaving 133,323 participants. We excluded subjects who had died, moved out of the study area, or were lost to follow-up before the 5-year follow-up. The response rate to the questionnaire was 81.1%.

Exposure assessment and covariates

The main independent variable in this study was rice compared with bread, noodle and cereal intake. Participants were asked about the frequency of consumption of individual food items as well as representative sizes relative to standard portions. Potential confounding variables included: age, obesity, tobacco consumption, alcohol consumption, physical activity, past history of type 2 diabetes, screening examinations for colorectal cancer, menopausal status and hormone use (women), intake of red meat, total energy, calcium, magnesium, vitamin B6, vitamin B12, folate, vitamin D, n-3 PUFAs, and fiber.

Outcome assessment

The main outcome variable in this study was colorectal cancer coded as C18-C20 and further divided into colon (C18.0–C18.5 for proximal colon and C18.6–C18.7 for distal colon) and rectal (C19 and C20) cancer according to the International Classification of Diseases for Oncology, third edition. Hospital records and population-based cancer registries in the study areas identified colorectal cancer incidence cases. Subjects were followed for move-out, death and occurrence of cancer from the 5-year follow-up survey (around 1995 and 1998 respectively) through December 31, 2008.

Statistical analysis

We excluded participants who had cancer before the starting point (n=4,086), were missing information for main exposure variables (n=1,030) or reported extreme total energy intakes (n=4,666). 88,722 participants were enrolled in our analysis. Subjects with missing values for covariates were excluded (n=15,221). Resulting in a final sample of 73,501. We calculated person-years of follow-up for each participant from the starting point to the date of CRC diagnosis, date of move-out, death, or end of the follow-up (31 December 2008), whichever came first. Using Cox proportional hazards models, risk as hazard ratios and 95% confidence intervals were calculated for developing CRC and its subsites for rice categories in quartiles by sex, with the lowest consumption category as

the reference, adjusted for potential confounding variables. All analyses were performed with Stata SE 12.1.

Results

1,276 colorectal cancer incident cases were identified during 801,937 person-years of follow-up. Age-adjusted colorectal cancer incidence ranged from 20.62 (highest quarter of rice) to 24.10 (lowest) per 1000 in men and 11.20 to 12.05 in women respectively. The multivariate HRs for the highest compared with the lowest quartile of rice in men was 0.77 (95% CI, 0.56-1.07). The trend analysis was not statistically significant. In women, no association was found for rice intake and colorectal cancer risk, however a non-significant trend between increased cereal intake and the risk of colorectal cancer was found. Further stratified analyses showed site-specific results: colon, rectum, proximal and distal colon cancer. We noted a non-significant inverse association between the quartiles of rice intake and the risk of rectal cancer in men. In women, a non-significant trend of risk increase by quartile of rice intake and proximal colon cancer was found, but not in men. Distal colon cancer showed no association with rice in both sexes. Sensitivity analyses were performed excluding intra mucosal/non-invasive cases however results were not substantially different. Effect modification for rice and major covariates was tested. Rice and smoking, alcohol consumption and BMI were significant in women. Subgroup analyses were also performed for smoking, alcohol, BMI, METS and past history of diabetes, but showed no significant colorectal cancer incidence risk difference between subcategories by rice consumption.

Conclusion

Our findings suggest that the consumption of rice does not have a substantial impact on the risk of colorectal cancer in the Japanese population, mainly non-metropolitan. Regarding the contradictory patterns between rice intake and colorectal cancer observed in Japan, within the JPHC Study context, rice intake might represent more than just a staple food. Previous research has linked rice with specific dietary patterns. These may further suggest variations in lifestyles attached to culture. The present study does not have a final answer to the interpretation of this contradiction. However, some insights were gained contributing to the body of knowledge in this field. For example, while results were overall non-significant some trends were implied: an inverse association between rice intake and colorectal cancer, specifically cancer of the rectum in men. While a positive association between rice intake and colorectal cancer especially pronounced in

proximal cancer of among women was suggested. These differences might explain the seemingly contradictory trends observed in Japan and may have biological or behavioral roots.

More meta-analyses and pooled studies, especially within Asian are needed to confidently interpret these results. Research on possible genetic risk and gene-environment interactions would also benefit the literature gap. This study, within the Japanese non-metropolitan setting, has shown that rice is neither hazardous nor protective of developing colorectal cancer. In a way this is a relief, Japanese should continue to enjoy their staple carbohydrate consumed with many different dishes. In the meantime, we as researchers can look to other potential risk factors.