

## 審査の結果の要旨

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The key research question of my study was: What is the association between rice and colorectal cancer compared with bread, noodle and cereal intake in Japanese men and women using Japan Public Health Center-based prospective Study data? The main objective of my study was, first to assess colorectal cancer risk by quartile of rice, bread, noodle, and carbohydrate intake; second to evaluate effect modification of main risk factors and rice on colorectal cancer; and finally to compare risk differences by colorectal cancer subsite and gender.

The key findings of my studies are as follows:

1. 1,276 new colorectal cancer cases (777 for men, 499 for women) were identified during 801,937 person-years of follow-up. Age-adjusted colorectal cancer incidence (per 1000) in men and women ranged from 20.62 (highest quarter of rice) to 24.10 (lowest) and from 11.20 to 12.05, respectively.
2. There was no statistically significant association between rice intake and colorectal cancer risk among men for the Hazard Ratios estimated in the full model including all possible confounding factors for the highest compared to the lowest quartile of rice in men: 0.77 (95% CI: 0.56-1.07). The trend analysis for quartiles of rice intake was not statistically significant. In women, no association was found for rice intake and colorectal cancer risk.
3. Further stratified analyses show site-specific results for colon and rectal cancer, respectively and proximal and distal colon cancers, respectively. 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 in colon

cancer 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. No clear patterns of association were observed in bread, noodle and cereal intake.

4. Effect modification for rice and major covariates was tested. No terms were significant for men, whereas a significant effect modification was found between rice and smoking, alcohol consumption, and BMI among women (P for interaction with rice was 0.004 for smoking, 0.02 for alcohol consumption and 0.02 for BMI). Subgroup analyses stratifying by gender and smoking (never vs ever) and alcohol (non-regular vs. regular), BMI (<25 vs. ≥25), METS (Q1&Q2 vs. Q3&Q4), past history of diabetes mellitus (no vs. yes), were performed individually, but showed no significant colorectal cancer incidence risk difference by quartiles of rice consumption in these subcategories.

To the best of our knowledge, this is the first population-based study on the association between rice intake and colorectal cancer in Japan. Overall rice intake was not associated with colorectal cancer and subsites within the Japan Public Health Center-based prospective Study. However some non-significant trends were implied: an inverse trend between rice intake and rectal cancer in men. In women non-significant results hinted at a positive with proximal colon cancer. No strong associations were found, therefore this study concludes that Japanese should continue to consume rice and that researchers should conduct pooled analysis and explore possible gene-environment interactions.