Title of research project	Cancer risk assessment of dietary acrylamide intake based on
	large-scale prospective cohort study, development of dietary
	acrylamide exposure assessment method, and evaluation of their
	validity
Research project no.	1503
Research period	FY 2015–2017
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RESEARCH REPORT - No. 1503 FY 2015-2017

[Abstract]

The goal of this study was to investigate the cancer risk of dietary acrylamide exposure in Japanese population. The study consisted of 3 aims: (1) To develop the methods of dietary exposure assessments such as dietary records (DR) and food frequency questionnaire (FFQ), and evaluate the validity of those methods using duplicate methods (DM) as a reference method; (2) To investigate the association between dietary intake of acrylamide and various cancer cases using the data of large-scale prospective cohort study; (3) To develop methods to measure the acrylamide-hemoglobin adduct level in blood, and compare the biomarker level with estimated dietary intake using DM and FFQ.

(1) Development of methods for estimation of acrylamide, and evaluation of their validity

A validation study was conducted on 14 participants from 11 households in the previous study in 2014. Food samples were simultaneously collected for DM and DR on the same day over 2 consecutive days. The FFQ was administered after collecting samples for DM and DR. For DM, dietary acrylamide was calculated from chemical analyses of each food. For DR and FFQ, the acrylamide intake through each food was calculated using the database on acrylamide contents in the foods. Correlation coefficients were calculated by the Spearman rank method.

As the results, average acrylamide intake values calculated using the DM, DR, and FFQ were 0.106, 0.233, and 0.128 μ g/kg body weight/day, respectively; these values showed a marginally positive correlation between the DM and DR, but a low correlation between the DM and FFQ. The result suggested that validity of acrylamide intake estimation using DR was reasonably high when compared to the analytical value obtained using simultaneously performed DM. However, further improvement is required for estimating acrylamide intake using FFQ. (2) Association between dietary intake of acrylamide and cancer development

Firstly, we validated a method to assess acrylamide exposure among the Japanese population using a FFQ from the Japan Public Health Center-based prospective study.

Validation studies for the FFQ were conducted in 1994 (n=215) and 1996 (n=350). The 28-day dietary records (DRs) were collected over 1 year. The FFQ was distributed before and after DR collection. Data for acrylamide exposure were based on reported measurements in Japan, and

calculations considered the cooking process for specific vegetables in a home setting. As the results, correlation coefficients varied from 0.37 to 0.54 depending on the area and sex. In conclusion, the FFQ was valid for use in epidemiological studies.

Secondly, we investigated the association between dietary acrylamide intake and risk of various cancer in the Japan Public Health Center-based Prospective Study, a large-scale cohort study in Japan. Dietary acrylamide intake was assessed using a validated FFQ.

As the results, dietary acrylamide intake was not associated with the risk of developing cancer in breast, ovarian, lung, esophagus, stomach, colorectal, renal, bladder and prostate. There were decreasing risk of endometrial and liver cancer, which relate to the protective effect of coffee intake. In conclusion, dietary acrylamide intake was not associated with the risk of most types of cancer in this population-based prospective cohort study of Japanese.

(3) Development of a method for measuring acrylamide-hemoglobin adduct level as a biomarker of dietary intake

We collected blood samples in 2015-16 from the 119 men and women who participated DM project conducted by Kawahara. et al¹⁰. In addition, we collected FFQ and urine samples. After a temporary freezing at -80 °C, we used erythrocyte to measure acrylamide-hemoglobin adduct level using the N-alkyl Edman method. We compared the level of acrylamide-hemoglobin adduct by tertiles of estimated acrylamide intake by DM and FFQ.

As the results, the level of acrylamide-hemoglobin adduct was highest in the highest tertile of intake estimated by DM and FFQ after adjusting sex and smoking status. The result suggested that acrylamide-hemoglobin adduct level may be used as a biomarker of dietary intake of acrylamide.

We established a method for preprocessing estimation of valine concentration in blood. We also established a new method by Edman procedure using a part of Hb protein as internal standard substance. In our research, there is no difference between male and female in the amount of AA-Val, but smoker has AA-Val more than non-smoker. And of the association between DM and amount of AA-Val in the group of blood sampled within 1 week was weaker than that in the other group.