Proceedings of the Nutrition Society (2024), **83 (OCE4)**, E427 doi:10.1017/S0029665124006657

Nutrition Society Congress 2024, 2–5 July 2024

Nitrosyl-heme and heme iron intake from processed meats and risk of colorectal cancer in the EPIC-Spain cohort

L. Rizzolo-Brime[1], L. Lujan-Barroso[1,2], A. Farran-Codina[3], R. Bou[4], C. Lasheras[5], P. Amiano[6,7,8], A. Aizpurua[7,8], M.J. Sánchez[6,9,10], E. Molina-Montes[6,10,11,12], M. Guevara[6,13,14], C. Moreno-Iribas[6,13,14], A. Gasque[13], M.D. Chirlaque-López[6,15,16], S.M. ColoradoYohar[6,15,17], J.M. Huerta[6,15], R. Zamora-Ros[1,18], A. Agudo[1] and P. Jakszyn[1,19]

[1]*Unit of Nutrition and Cancer, Epidemiology Research Programme, Catalan Institute of Oncology (ICO), Bellvitge Biomedical Research Institute (IDIBELL), 08908 L'Hospitalet de Llobregat, Spain*

[2]*Department of Public Health, Mental Health and Maternal and Child Health Nursing. Faculty of Nursing. University of Barcelona, Carrer de la Feixa Llarga s/n, 08907, L'Hospitalet de Llobregat, Barcelona, Spain*

[3]*Department of Nutrition, Food Science and Gastronomy, Faculty of Pharmacy, Institute of Nutrition and Food Safety (INSA-UB), University of Barcelona, Campus de l'Alimentació de Torribera, Av. Prat de la Riba 171, Santa Coloma de Gramenet, E-08921 Barcelona, Spain*

[4]*Food Safety and Functionality Program, Institute of Agrifood Research and Technology (IRTA), Finca Camps i Armet s/n, 17121- Monells, Girona, Spain*

[5]*Functional Biology Department, School of Medicine, University of Oviedo, Asturias, Spain*

[6]*Spanish Consortium for Research on Epidemiology and Public Health (CIBERESP), Instituto de Salud Carlos III, Madrid, Spain*

[7]*Ministry of Health of the Basque Government, Sub Directorate for Public Health and Addictions of Gipuzkoa, San Sebastian, Spain*

[8]*BioGipuzkoa (BioDonostia) Health Research Institute, Epidemiology of Chronic and Communicable Diseases Group, San Sebastián, Spain*

[9]*Escuela Andaluza de Salud Pública (EASP), 18011 Granada, Spain*

[10]*Instituto de Investigación Biosanitaria ibs.GRANADA, 18012 Granada, Spain*

[11]*Department of Nutrition and Food Science, Campus of Cartuja, University of Granada, 18071 Granada, Spain*

[12]*Institute of Nutrition and Food Technology (INYTA) 'José Mataix', Biomedical Research Centre, University of Granada, 18071 Granada, Spain*

[13]*Instituto de Salud Pública y Laboral de Navarra, 31003 Pamplona, Spain*

[14]*Navarra Institute for Health Research (IdiSNA), 31008 Pamplona, Spain*

[15]*Department of Epidemiology, Murcia Regional Health Council-IMIB, Murcia, Spain*

[16]*Social-Health Department, Murcia University, 30008 Murcia, Spain*

[17]*Research Group on Demography and Health, National Faculty of Public Health, University of Antioquia, Medellín, Colombia*

[18]*Department of Nutrition, Food Sciences, and Gastronomy, Food Innovation Network (XIA), Institute for Research on Nutrition and Food Safety (INSA), Faculty of Pharmacy and Food Sciences University of Barcelona, Barcelona, Spain*

[19]*Blanquerna School of Health Sciences, Ramon Llull University, 08022 - Barcelona, Spain*

The International Agency for Research on Cancer classified processed meats (PMs) as "carcinogenic" and red meat as "probably carcinogenic" for humans[(1)]. The possible relationship between colorectal cancer (CRC) risk and processed meats (PMs), along with the specific compound contributing to this association have not been established yet. Nitrosyl-heme and heme iron have been proposed as potential-related compounds. The aim of this study was to assess the association of nitrosyl-heme and heme iron intake with CRC risk among participants from the European Prospective Investigation into Cancer and Nutrition (EPIC) Spain study.

This prospective study included 38,262 subjects (61.5% females) from the EPIC-Spain study. Food consumption was assessed by a validated diet history questionnaire[(2)]. Dietary intake of nitrosylheme and heme iron was estimated by matching PMs intake and composition data based on laboratory analyses conducted using a High Performance Liquid Chromatography method[(3)]. In brief, the daily intake of nitrosyl-heme and heme iron was determined by multiplying the intake of each PM (in grams/day) by its corresponding content of nitrosyl-heme and heme iron, and then summing up the estimated intakes from all PMs. The proportional hazards models were used to examine the association between sex-specific tertiles of nitrosyl-heme and heme iron intake and CRC risk and 95%

confidence intervals (CIs) were computed using Cox regression. Age served as the time scale, stratified by age and centre with adjustments for sex, energy intake, body mass index (BMI), waist circumference, education, smoking, physical activity in MET-h/week, lifetime alcohol consumption, dietary fibre, calcium intake, and family CRC history. Homogeneity of location subtype risk was also assessed. Interactions with smoking, BMI, physical activity, and alcohol were examined and sensitivity analyses were also conducted excluding the first three years of follow-up.

During a mean follow-up of 16.7 years, 577 CRC were identified. We found no overall association between nitrosyl-heme (T3 vs T1; HR: 0.98 (95% CI: 0.79-1.21)) or heme iron intakes (T3 vs T1; HR: 0.88 (95% CI: 0.70-1.10)) with CRC risk, nor according to tumour subtypes. However, we found a non-statistically significant positive association between nitrosyl-heme intake and proximal colon, HR = 1.03; 95% CI, (0.65-1.61) and rectum cancer, HR = 1.04; 95% CI, (0.70-1.56).

Our study found no evidence supporting a link between nitrosyl-heme or heme iron intake and CRC risk in Spanish subjects from the EPIC cohort. As these results are novel and preliminary, more heterogeneous studies are necessary to provide more convincing evidence on their role in colorectal carcinogenesis.

Acknowledgments

This study was supported by Instituto de Salud Carlos III through the PI19/00817 project (cofunded by the European Regional Development Fund (ERDF), a way to build Europe) and through the PFIS FI20/00006 predoctoral funding (co-funded by the European Social Fund (ESF), investing in your future). The coordination of EPIC is financially supported by the European Commission (DG-SANCO) and the International Agency for Research on Cancer. This study is part of the EPIC-Spain Study. The EPIC-Spain cohort was supported by the Health Research Fund (FIS) - Instituto de Salud Carlos III (ISCIII), the Regional Governments of Andalucía, Asturias, Gipuzkoa, Murcia and Navarra, and the Catalan Institute of Oncology (ICO). We thank CERCA Programme/Generalitat de Catalunya for institutional support.

References

1. IARC Working group (2015). Carcinogenicity of consumption of red and processed meat [Available from: https://www.thelancet.com/oncology].
2. Riboli E, Hunt KJ *et al* (2002) *Public Health Nutr* **5**(6B), 1113–24.
3. Bou R., Farran-Codina A, Rizzolo-Brime L *et al* (2024) *J Food Compos & Anal* **125**(105832), 105832.