Environment International 121 (2018) 428–434

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

# Colorectal cancer, sun exposure and dietary vitamin D and calcium intake in the MCC-Spain study

Xavier Vallès[a,b], M. Henar Alonso[a,b,c], Juan Francisco López-Caleya[d,e], Virginia Díez-Obrero[a,c], Trinidad Dierssen-Sotos[b,f], Virginia Lope[b,g], Ana Molina-Barceló[h], María Dolores Chirlaque[b,i,j], José Juan Jiménez-Moleón[b,k,l], Guillermo Fernández Tardón[b,m], Jesús Castilla[b,n], Pilar Amiano[b,o], Rocío Capelo[p], Gemma Castaño-Vinyals[b,q,r,s], Elisabet Guinó[a,b], Antonio José Molina de la Torre[d], Conchi Moreno-Iribas[b,n], Beatriz Pérez Gómez[b,g], Nuria Aragonés[b,t], Javier Llorca[b,f], Vicente Martín[b,d], Manolis Kogevinas[b,q,r,s], Marina Pollán[b,g], Victor Moreno[a,b,c,*]

[a] Cancer Prevention and Control Program, Catalan Institute of Oncology (ICO) and Oncobell Program, Bellvitge Biomedical Research Institute (IDIBELL), L'Hospitalet de Llobregat, Barcelona, Spain
[b] Consortium for Biomedical Research in Epidemiology and Public Health (CIBERESP), Madrid, Spain
[c] Department of Clinical Sciences, Faculty of Medicine and Health Sciences, University of Barcelona, Barcelona, Spain
[d] Instituto de Biomedicina (IBIOMED), Universidad de León, Spain
[e] Servicio de Medicina Interna, Hospital de Cabueñes, Gijón, Asturias, Spain
[f] Universidad de Cantabria - IDIVAL, Santander, Spain
[g] Environmental and Cancer Epidemiology Unit, National Center of Epidemiology, Instituto de Salud Carlos III, Madrid, Spain
[h] Área de Cáncer y Salud Pública, FISABIO-Salud Pública, Valencia, Spain
[i] Department of Epidemiology, Murcia Regional Health Council, IMIB-Arrixaca, Murcia, Spain
[j] Department of Health and Social Sciences, Universidad de Murcia, Murcia, Spain
[k] Department of Preventive Medicine and Public Health, Faculty of Medicine, University of Granada, Spain
[l] Instituto de Investigación Biosanitaria de Granada ibs.GRANADA, Hospitales Universitarios de Granada, Universidad de Granada, Granada, Spain
[m] Oncology Institute IUOPA (Instituto Universitario de Oncología del Principado de Asturias), Universidad de Oviedo, Asturias, Spain
[n] Instituto de Salud Pública Navarra - IdiSNA, Pamplona, Navarra, Spain
[o] Public Health Division of Gipuzkoa, BioDonostia Research Institute, San Sebastián, Spain
[p] Centro de Investigación en Recursos Naturales, Salud, y Medio Ambiente (RENSMA), Universidad de Huelva, Huelva, Spain
[q] ISGlobal, Barcelona, Spain
[r] IMIM (Hospital del Mar Medical Research Institute), Barcelona, Spain
[s] Universitat Pompeu Fabra (UPF), Barcelona, Spain
[t] Epidemiology Section, Public Health Division, Department of Health of Madrid, Madrid, Spain

ARTICLE INFO

Handling Editor: Yong Guan Zhu

*Keywords:*
Colorectal cancer
Sunlight
Calcium
Vitamin D
Skin phenotype

ABSTRACT

*Objectives:* To explore the association of colorectal cancer with environmental solar radiation and sun exposure behavior, considering phenotypic variables (eye color, hair color and skin phenotype), dietary intake of vitamin D and calcium, and socio-demographic factors.

*Study design:* Multicenter population-based frequency matched case-control study in Spain (MCC-Spain), with 2140 CRC cases and 3950 controls.

*Methods:* Data were obtained through personal interviews using a structured epidemiological questionnaire that included socio-demographic data, residential history, environmental exposures, behavior, phenotypic and dietary information. An environmental-lifetime sun exposure score was constructed combining residential history and average daily solar radiation, direct and diffuse. Logistic regression was used to explore the association between different variables. A structural equation model was used to verify the associations of the conceptual model.

*Results:* We found a lower risk of CRC in subjects frequently exposed to sunlight during the previous summer and skin burning due to sun exposure. No association was observed in relation to the residential solar radiation scores. Subjects with light eye or light hair colors had a lower risk of CRC that those with darker colors. Dietary calcium and vitamin D were also protective factors, but not in the multivariate model. The structural equation model analysis suggested that higher sun exposure was associated with a decreased risk of CRC, as well as

* Corresponding author at: Cancer Prevention and Control Program, Catalan Institute of Oncology, Gran Via 119-203, 08907 L'Hospitalet de Llobregat, Spain.
*E-mail address:* v.moreno@iconcologia.net (V. Moreno).

https://doi.org/10.1016/j.envint.2018.09.030
Received 19 June 2018; Received in revised form 17 September 2018; Accepted 17 September 2018

dietary intake of calcium and vitamin D, and these factors are correlated among themselves and with environmental solar radiation and skin phenotypes.
*Conclusion:* The results agree with previous observations that sun exposure, dietary vitamin D and calcium intake, and serum 25(OH)D concentration reduce the risk of CRC and indicate that these factors may be relevant for cancer prevention.

## 1. Introduction

Colorectal cancer (CRC) is the most frequent intestinal cancer worldwide, accounting for 447,000 incident cases in 2012 and 215,000 deaths in Europe (Arnold et al., 2013; Ferlay et al., 2013; Forman, 2010). Risk factors for CRC include advanced age, medical history of benign adenomatous polyps, inflammatory bowel diseases, diabetes, family history of CRC, low intake of vegetables and fruits, and high intake of dietary fat and processed meat (Potter, 2008; van Duijnhoven et al., 2009; Weitz et al., 2005). There is growing evidence of the association between sun exposure and CRC (van der Rhee et al., 2013). The association of sun exposure and cancer was initially proposed > 80 years ago by Peller, who had observed that occupations with a high incidence of skin cancer, like US Navy personnel, had a lower rate of other cancers (Peller, 1936; Peller and Stephenson, 1937). Following this hypothesis, Apprely described a reduced cancer mortality in North America in relation to solar radiation (Apprely, 1941). Since exposure to ultraviolet-B radiation from the sun produces vitamin D, and this vitamin is involved in calcium absorption, it has been hypothesized that this effect could be mediated through calcium and vitamin-D metabolism (Garland and Garland, 1980), an approach that has been supported by subsequent research (Di Rosa et al., 2013; Hart et al., 2011; Moukayed and Grant, 2017). All these factors, including behavioral, life-style and genetic background, may be interrelated and cross-influenced.

Here we have analyzed the association of CRC with the sun exposure and life-style, considering skin, hair and eye color phenotypes, dietary vitamin D and calcium intake, and other socio-demographic factors in a large multicenter case-control study conducted in Spain.

## 2. Methods

### 2.1. Study design and data collection

MCC-Spain is a population-based multicenter case-control study carried out between September 2008 and November 2014 in 12 Spanish provinces (Castano-Vinyals et al., 2015). The study included 6090 participants: 2140 CRC cases and 3950 controls (see Table 1). Cases

**Table 1**
Baseline characteristics of cases and controls.

| | Controls | Cases | OR[a] (95% CI) | P value |
|---|---|---|---|---|
| Age | | | | |
| Mean (SD) | 63.3 (11.8) | 67.0 (10.8) | 1.03 (1.02–1.03) | < 0.001 |
| Sex. N (%) | | | | |
| Male | 2018 (51.1) | 1365 (63.8) | 1 | < 0.001 |
| Female | 1932 (48.9) | 775 (36.2) | 0.59 (0.53–0.66) | |
| Education. N (%) | | | | |
| Basic | 739 (18.9) | 689 (32.2) | 1 | < 0.001 |
| Primary | 1273 (32.6) | 811 (37.9) | 0.68 (0.60–0.78) | |
| Secondary/Professional | 1108 (28.3) | 427 (20.0) | 0.41 (0.35–0.48) | |
| University | 789 (20.2) | 212 (9.9) | 0.28 (0.24–0.35) | |
| History of CRC in first-degree relatives. N (%) | | | | |
| No | 3483 (88.2) | 1663 (77.7) | 1 | < 0.001 |
| Yes | 467 (11.8) | 477 (22.3) | 2.36 (2.04–2.74) | |
| Diabetes. N (%) | | | | |
| No | 3352 (85.2) | 1739 (81.8) | 1 | 0.91 |
| Yes | 582 (14.89) | 386 (18.2) | 0.99 (0.85–1.15) | |
| Acetylsalicylic acid (ASA). N (%) | | | | |
| Non-use/sporadically use | 3068 (77.7) | 1698 (79.4) | 1 | 0.01 |
| Regular use in the last year | 880 (22.3) | 440 (20.6) | 0.82 (0.71–0.94) | |
| Nonsteroidal anti-inflammatory drugs (NSAID). N (%) | | | | |
| Non-use/sporadically use | 2718 (68.8) | 1715 (80.2) | 1 | < 0.001 |
| Regular use in the last year | 1230 (31.2) | 423 (19.8) | 0.62 (0.54–0.79) | |
| Physical activity in leisure time (MET). N (%) | | | | |
| No | 1633 (41.8) | 1100 (51.4) | 1 | < 0.001 |
| Yes | 2274 (58.2) | 1039 (48.6) | 0.70 (0.63–0.79) | |
| Body Mass Index at age 45 | | | | |
| Mean (SD) | 25.3 (4.1) | 26.1 (5.0) | 1.03 (1.02–1.04) | < 0.001 |
| Alcohol | | | | |
| Low consumption | 2809 (83.2) | 1386 (75.3) | 1 | < 0.001 |
| High consumption | 569 (16.8) | 455 (24.7) | 1.48 (1.27–1.71) | |
| Intake of vegetables (g/day) | | | | |
| Mean (SD) | 189.0 (123.4) | 174.6 (113.5) | 0.86 (0.81–0.90)[b] | < 0.001 |
| Intake of red meat (g/day) | | | | |
| Mean (SD) | 62.2 (39.4) | 73.8 (49.7) | 1.84 (1.59–2.14)[b] | < 0.001 |
| Intake of cured meat (g/day) | | | | |
| Mean (SD) | 17.4 (16.1) | 21.4 (22.2) | 2.42 (1.73–3.42)[b] | < 0.001 |
| Energy (kcal/day) | | | | |
| Mean (SD) | 1893.4 (637.6) | 2007.9 (710.0) | 1.25 (1.14–1.37)[b] | < 0.001 |

[a] The OR are adjusted for design variables (age, sex and recruiting center).
[b] The summary OR per 100 g/day and 1000 kcal/day.