THIRD PAGE: Abstract and keywords

Title: Population-based multicase-control study in common tumours in Spain (MCC-Spain): rationale and study design

Abstract

Background. We present the protocol of a large population-based case-control study of 5 common tumours in Spain (MCC-Spain) that evaluates environmental exposures and genetic factors.

Methods/Design. Between 2008-2013, ~~10,183~~10,106 subjects aged 20-85 were enrolled in 23 hospitals and primary care centres in 12 Spanish provinces including ~~1,115~~1,112 cases with a new diagnosis of prostate cancer, ~~1,750~~1,738 of breast cancer, ~~2,171~~2,140 of colorectal cancer, ~~492~~ 459 of gastro-oesophageal cancer, ~~554~~ 559 cases with chronic lymphocytic leukaemia (CLL) and 4,~~101~~ 098 population controls frequency matched to cases by age, sex and region of residence. Participation rates ranged from 57% (stomach cancer) to 87% (CLL cases) and from 30% to 77% in controls. Participants completed a face-to-face computerized interview on sociodemographic factors, environmental exposures, occupation, medication, lifestyle, personal and family medical history. In addition, subjects completed a self-administered food-frequency questionnaire and telephone interviews. Blood samples were collected from 76% of subjects while saliva samples were collected for CLL cases and participants refusing blood drawing. Clinical information was recorded for cases and paraffin blocks and/or fresh tumour samples are available in most collaborating hospitals. Genotyping was done through an exome array enriched with genetic markers in specific pathways. Multiple analyses are planned to assess the association of environmental, personal and genetic risk factors for each tumour and identify pleiotropic effects.

Discussion. This study, conducted within the Spanish Consortium for Biomedical Research in Epidemiology & Public Health (CIBERESP), is a unique initiative to evaluate etiological factors for common cancers and will promote cancer research and prevention in Spain.

Keywords: Case-control, epidemiology, colorectal cancer, prostate cancer, breast cancer, gastric cancer, chronic lymphocytic leukemia.

THIRD PAGE: Abstract and keywords (in Spanish)

Título: Estudio multicaso-control de base poblacional de tumores comunes en España (MCC-Spain): razón y diseño del estudio

Resumen

Introducción. Presentamos el protocolo del estudio caso-control de base poblacional de 5 tumores comunes en España (MCC-Spain) que evalúa factores ambientales y genéticos.

Métodos. Durante 2008-2013, se reclutaron ~~10.183~~ 10.106 sujetos entre 20-85 años en 23 hospitales de 12 provincias españolas, incluyendo 1.~~115~~ 112 casos de cáncer de próstata, 1.~~750~~ 738 de mama, 2.~~171~~ 140 colorrectal, ~~492~~ 459 gastro-esofágicos, ~~554~~ 559 de leucemia linfática crónica (LLC) y 4.~~101~~ 098 controles poblacionales emparejados por frecuencia por edad, sexo y región de residencia. Las tasas de participación varían del 57% (cáncer de estómago) al 87% (casos de LLC) y del 30% al 77% en controles. Los participantes respondieron una entrevista personal informatizada sobre factores socio-demográficos, exposiciones ambientales, ocupación, medicación, estilos de vida, e historia médica personal y familiar. Además, cumplimentaron un cuestionario alimentario y realizaron entrevistas telefónicas. Se recogió sangre del 76% de los participantes y saliva para los casos de LLC y participantes que rechazaron la donación de sangre. En los casos, se recogió información clínica y se dispone de muestras de tumor fresco o parafinado a través de los biobancos de los hospitales. Se realizó el genotipado con un array de exoma suplementado con marcadores en pathways específicos. Se han planificado diversos análisis para evaluar la asociación de factores genéticos, personales y ambientales para cada tumor e identificar efectos pleiotrópicos.

Discusión. Este estudio, desarrollado en el Consorcio de Investigación Biomédica de Epidemiología y Salud Pública (CIBERESP), es una iniciativa única para evaluar factores etiológicos de tumores comunes y promoverá la investigación en cáncer y prevención en España.

Palabras clave: Caso-control, epidemiología, cáncer colorrectal, cáncer de próstata, cáncer de mama, cáncer gástrico, leucemia linfática crónica.

METHODS

1. Study design

MCC-Spain is a population-based multicase-control study carried out between September 2008 and December 2013 in 12 Spanish provinces (Asturias, Barcelona, Cantabria, Girona, Granada, Gipuzkoa, Huelva, León, Madrid, Murcia, Navarra and Valencia). Recruitment of cases and controls was performed simultaneously: study personnel contacted newly diagnosed cancer cases in the 23 collaborating hospitals, and invited through the telephone population controls, who had been randomly selected from the administrative records of selected primary care health centres located within these hospitals' catchment area. In total, the study recruited 10,~~183~~ 106 subjects (Table 1). All participants had to be 20-85 years, to have resided in the catchment area for at least 6 months prior to recruitment, and to be able to answer the epidemiological questionnaire. Each province recruited cases of at least two different tumour sites. Cases were identified, as soon as possible after the diagnosis was made, through active search that included periodical visits to the collaborating hospital departments (i.e. gynaecology, urology, gastroenterology, oncology, general surgery, radiotherapy, and pathology departments). We included histologically confirmed incident cases of cancer of the prostate (International Classification of Diseases 10th Revision [ICD-10]: C61, D07.5), breast (C50, D05.1, D05.7), colon or rectum (C18, C19, C20, D01.0, D01.1, D01.2), stomach (C16, D00.2), lower third of the oesophagus (C15.5), or chronic lymphocytic leukaemia and small lymphocytic lymphoma (C91.1), with no prior history of the disease, and diagnosed within the recruitment period, which differed by province; in CLL prevalent cases were also recruited. Controls were frequency-matched to cases, by age, sex and region, ensuring that in each region there was at least one control of the same sex and 5-year interval for each case. For each control needed, a total of five potential participants of similar age, sex and hospital catchment area were randomly selected from the general practitioner lists. If contact with the first person of this list was not possible after a minimum of five tries at different times of the day, or if he/she refused to participate, the following person of the list was approached.

Table 1. Number of cases and controls with complete interviews by tumour type and geographic area.

Area (number of hospitals)	Controls	Colorectal	Breast	Prostate	Stomach / Oesophagus	CLL	Total	Start (month/year)	Finish (month/year)
Asturias (2)	232	77	70	16	14	53	462	11/08	02/12
Barcelona (4)	1,036	696	292	404	100	407	2,935	09/07	12/13
Cantabria (1)	377	151	141	175	24	22	890	04/10	07/12
Girona (2)	82		47			30	159	03/12	07/13
Granada (2)	187	164		64	5	47	467	04/10	06/13
Gipuzkoa (2)	362	119	226				707	02/08	07/10
Huelva (2)	177	71	108	52	15		423	04/10	05/13
León (1)	441	390	226	0	123		1,180	02/09	06/12
Madrid (2)	733	232	341	315	110		1,731	12/08	05/12
Murcia (1)	42	34			1		77	02/08	06/10
Navarra (2)	274	125	226		53		678	10/08	03/11
Valencia (2)	155	81	61	86	14		397	07/10	04/12
TOTAL	4,098	2,140	1,738	1,112	459	559	10,106	09/07	12/13

Table 2. Main characteristics of the population of the MCC-Spain study

	Controls	Colorectal	Breast	Prostate	Stomach/ Esophagus	CLL
	N=4098	N=2140	N=1738	N=1112	N=459	N=559
Area:						
Asturias	232 (5.7%)	77 (3.6%)	70 (4%)	16 (1.4%)	14 (3.1%)	53 (9.5%)
Barcelona	1036 (25.3%)	696 (32.5%)	292 (16.8%)	404 (36.3%)	100 (21.8%)	407 (72.8%)
Cantabria	377 (9.2%)	151 (7.1%)	141 (8.1%)	175 (15.7%)	24 (5.2%)	22 (3.9%)
Girona	82 (2%)		47 (2.7%)			30 (5.4%)
Granada	187 (4.6%)	164 (7.7%)		64 (5.8%)	5 (1.1%)	47 (8.4%)
Gipuzkoa	362 (8.8%)	119 (5.6%)	226 (13%)			
Huelva	177 (4.3%)	71 (3.3%)	108 (6.2%)	52 (4.7%)	15 (3.3%)	
León	441 (10.8%)	390 (18.2%)	226 (13%)		123 (26.8%)	
Madrid	733 (17.9%)	232 (10.8%)	341 (19.6%)	315 (28.3%)	110 (24%)	
Murcia	42 (1%)	34 (1.6%)			1 (0%)	
Navarra	274 (6.7%)	125 (5.8%)	226 (13%)		53 (11.5%)	
Valencia	155 (3.8%)	81 (3.8%)	61 (3.5%)	86 (7.7%)	14 (3.1%)	
Sex:						
Men	2060 (50.3%)	1365 (63.8%)		1112 (100%)	308 (67.1%)	335 (59.9%)
Women	2038 (49.7%)	775 (36.2%)	1738 (100%)		151 (32.9%)	224 (40.1%)
Age (mean(sd))	62.9 (12.1)	67.0 (10.8)	56.4 (12.6)	66.1 (7.33)	66.4 (12.4)	66.2 (10.2)
Education:						
Less than primary school	753 (18.4%)	688 (32.1%)	270 (15.5%)	261 (23.5%)	138 (30.1%)	152 (27.2%)
Primary school	1306 (31.9%)	806 (37.7%)	563 (32.4%)	439 (39.5%)	177 (38.6%)	161 (28.8%)
Secondary school	1182 (28.8%)	426 (19.9%)	574 (33.0%)	242 (21.8%)	96 (20.9%)	148 (26.5%)
University	857 (20.9%)	220 (10.3%)	331 (19.0%)	170 (15.3%)	48 (10.5%)	98 (17.5%)
Race:*						
White	4031 (98.5%)	2116 (98.9%)	1692 (97.4%)	1096 (98.6%)	443 (96.7%)	554 (99.3%)
Nonwhite	60 (1.47%)	24 (1.12%)	46 (2.65%)	16 (1.44%)	15 (3.28%)	4 (0.72%)