BRIEF ORIGINAL

CANCER SURVIVAL (1995-2004) IN THE BASQUE COUNTRY, SPAIN

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ABSTRACT

Background: geographic differences described in the prognosis of cancer patients in the Basque Country have been attributed to a different incidence in tumours with different lethality. Therefore, cancer relative survival adjusted by case-mix was included to estimate cancer survival by provinces and health regions, using data from 1995 to 2004.

Methods: a total of 93 585 cases of malignant tumours were identified from a population-based cancer registry. The five-year relative survival (RS) was calculated using Ederer´s method. The five-year relative excess risk (RER) of death was estimated with a generalised linear model, standardized by age and adjusted for sex, date of diagnosis and case-mix.

Results: the five-year RS increased from period 1995-1999 to 2000-2004, this latter, with values ranging by health regions between 46-58% and 57-65% in men and women, respectively. There was an excess risk of death in Bizkaia (RER=1.06, CI95%: 1.03-1.09), this same effect being identified in almost all the health regions in the province. In contrast, in Gipuzkoa province, differences were only statistically significant in the Gipuzkoa and Tolosa health regions (RER=1.07; CI95%: 1.02-1.13 and RER=0.91; CI95%: 0.84-0.98, respectively), and even these disappeared after adjusting for potential confounders.

Conclusions: cancer patients of Bizkaia, except for the Uribe health region, presented a worse prognosis.

Key words: Survival. Cancer. Cancer registry. Spain.

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RESUMEN

Supervivencia del cáncer en el País Vasco entre 1995 y 2004

Fundamentos: las diferencias geográficas descritas en el pronóstico de los pacientes de cáncer en el País Vasco han sido atribuidas a la diferente incidencia en tumores de diferente letalidad. Por ello, se incluye la supervivencia relativa del cáncer ajustada por la casuística para estimar la supervivencia del conjunto de los tumores malignos por provincias y comarcas sanitarias, utilizando los datos de 1995 a 2004. El objetivo del trabajo es estimar la supervivencia de los tumores malignos en el País Vasco por provincias y comarcas sanitarias durante el período 1995-2004.

Métodos: se incluyeron 93.585 tumores malignos del registro poblacional de cáncer. Se calculó la supervivencia relativa (SR) a 5 años con el método de Ederer. Se estimó el exceso de riesgo relativo (ERR) de muerte a los 5 años con el modelo lineal generalizado, estandarizando por edad y ajustando por sexo, período de diagnostico y casuística.

Resultados: la SR a los 5 años aumentó en el período 2000-2004 con respecto a 1995-1999 con valores que oscilaron por comarcas entre el 46-58% y el 57-65% en hombres y mujeres, respectivamente. Se observó un exceso de riesgo de muerte en pacientes de Bizkaia (ERR= 1,06; IC95%: 1,03-1,09, efecto que se observo en casi todas sus comarcas. Por el contrario, en Gipuzkoa, sólo las comarcas Gipuzkoa y Tolosa mostraron diferencias significativas (ERR=1,07; IC95%: 1,02-1,13 y ERR=0,91; IC95%: 0,84-0,98, respectivamente), las cuales desaparecieron al ajustar el modelo.

Conclusiones: dentro del Pais Vasco fueron los pacientes de Bizkaia, a excepción de la comarca Uribe, los que presentaron peor pronóstico.

Palabras clave: Supervivencia. Cáncer. Registros de cáncer.

INTRODUCTION

In recent decades, there has been an increase in cancer survival in Europe overall[1,2] and in the Basque Country[3] as well, mainly due to improvements in the diagnosis and treatment of the disease. However, differences in survival have been found not only between countries[2,4], but also between regions within a country[2,5]. In the Basque Country, differences have been found at province level, with survival being the lowest in Bizkaia[3]. However, there are no studies in Spain about what happens in small areas such as health region.

Cancer population-based registries allow to study survival in all types of cancers in a given geographical area and give us an indirect measure of the performance of the health system in the area of oncology. However, this assessment may be distorted by the fact that the incidence of particularly lethal forms of cancer may be higher in one geographical area than another, due to different risk factors. A solution to eliminate this effect is raised by several European studies[2,6,7], in which cancer relative survival is adjusted by case-mix (cancer site).

The objective of this study was to assess survival of malignant tumours in the Basque Country between 1995 and 2004 by provinces and health regions.

MATERIAL AND METHODS

Study population

Data were obtained from the Basque Cancer Registry (BCR). Their sources of information are the hospital cancer registries from Osakidetza and Oncological Institute, other public, private and/or subcontracted hospital, clinics or laboratories concerned with the diagnosis and treatment of cancer and death certificates. All cases of cancer diagnosed in adults (>14 years old) residents in the Basque Country in the period 1995-2004 were included. Cases for which the only source of information was the death certificate (DCO) were excluded, as were those diagnosed at autopsy and all secondary and successive tumours. The vital status (alive, dead or lost to follow-up) was completed by a linkage with the national death index and with an active follow-up in several sources of information (hospital clinical records, national death index and individual health cards). All cases not deceased, with a follow-up lower than 5 years, were censored.

Statistical analysis

The following explanatory variables were considered: age, with five groups (15-44, 45-54, 55-64, 65-74 and >74 years old); period of diagnosis (1995-1999 or 2000-2004); location of the cancer (case-mix), coded according to the 10th revision of the International Classification of Diseases (ICD-10)8 and classified into five categories according to the average five-year survival rate in Europe1 (table 1) plus an additional category that included other locations not added in the previous categories and ill-defined sites. Finally, province (Araba, Gipuzkoa and Bizkaia) and health region of residence (in Araba province: Araba; in Gipuzkoa province: Alto Deba, Bajo Deba, Donostia, Bidasoa, Gipuzkoa, Goierri and Tolosa; in Bizkaia province: Interior, Portugalete-Enkarterri, Barakaldo-Sestao, Uribe and Bilbo) were considered.

Relative survival (RS) is the ratio between the observed survival (OS), calculated using the Kaplan-Meier estimator, and the expected survival, estimated from the mortality in the general popula-

Table 1
Groupings of malignant tumours by relative survival rates found in EUROCARE-3, for adjusting for case-mix

Primary tumour (according to site)	Código CIE-10	Categoría
Lip, melanoma, testis, thyroid gland, Hodgkin lymphoma	C00 C43 C62 C73 C81	1
Larynx, breast, cervix uteri, corpus uteri, uterus NOS, female genital organs NOS, penis, prostate, ureter, bladder.	C32 C50 C53 C54 C55 C57 C60 C61 C66 C67	2
Tongue NOS, gum, floor of mouth, palate, mouth NOS, parotid gland, major salivary gland and NOS, tonsil, nasopharynx; piriform sinus, colon, rectosigmoid junction, nasal cavity and middle ear, bone and articular cartilage of limbs, other bones and NOS, Kaposi´s sarcoma, peripheral nerves and autonomic nervous system, retroperitoneum and peritoneum, other connective and soft tissue, vulva, vagina, kidney (except renal pelvis), renal pelvis, urinary organs NOS, follicular lymphoma, non-follicular lymphoma, mature T/NK-cell lymphoma, non-Hodgkin lymphoma NOS, malignant immunoproliferative diseases.	C02 C03 C04 C05 C06 C07 C08 C09 C11 C12 C18 C19 C30 C40 C41 C46 C47 C48 C49 C51 C52 C64 C65 C68 C82 C83 C84 C85 C88	3
Base of tongue, oropharynx, hypopharynx, stomach, small intestine, ovary, multiple myeloma and malignant plasma cell neoplasm, lymphoid leukaemia, myeloid leukaemia, monocytic leukaemia, other leukaemias of specified cell type, leukaemia of unspecified cell type, lymphoid and haematopoietic and related tissue NOS.	C01 C10 C13 C16 C17 C56 C90 C91 C92 C93 C94 C95 C96	4
Oesophagus, anus and anal canal, liver and intrahepatic bile ducts, gallbladder, bile tract NOS, pancreas, trachea, lung, heart, mediastinum and pleura, mesothelioma, eye and adnexa, meninges, brain, spinal cord, cranial nerves and other parts of central nervous system.	C15 C21 C22 C23 C24 C25 C33 C34 C38 C45 C69 C70 C71 C72	5
Other sites not included in the 5 previous categories and ill-defined sites of different organs: lip, oral cavity and pharynx NOS, rectum, digestive organs NOS, accessory sinuses, thymus, thorax NOS, placenta, male genital organs NOS, adrenal gland, endocrine glands and related structures, ill-defined sites, without specification of site.	C14 C20 C26 C31 C37 C39 C58 C63 C74 C75 C76 C80	6

ICD-10: 10th edition of the International Classification of Diseases. Created from figure 2 of Coleman MP et al 2003 article.

tion. The five-year RS was calculated, with its 95% confidence interval, using Ederer´s method9. We used specific life tables by age (year-to-year) and by sex for the general population in the area under study, that is, for the Basque Country, each province and each health region, and for the periods 1995-1999, 2000-2004 and 2005-2009. These tables were constructed from the mortality and population data for each geographical area. For provinces and health regions, life tables were smoothed by the Elandt-Johnson method[10,11], grouping data by age in five-year intervals, to then estimate complete tables. Finally, the RS was standardised by age using the Brenner method[12], and weighted as proposed by Corazziari[13], to produce a single standard, without distinguishing between different types of cancer. Based on these results, we used generalised linear models14 to assess the five-year relative excess risk (RER) attributable to the province and health region of residence, adjusting for the following variables:

sex, date of diagnosis (model 1) and case-mix (model 2).

Statistical analysis was carried out using the Stata software package (version 10) with the strs15 and strel16 macros.

RESULTADOS

A total of 93,585 cases of malignant cancer (60.1% men) were identified, of which 43,441 from the period 1995-1999 and 50,144 from 2000-2004. In 87.1% and 88.3% of cases, cyto-histological verification was available in the first and second period, respectively (Goierri and Bilbao health regions are around 84%). The 4.3% of cases in 1995-1999 and 2.7% (which is more than 4% in Tolosa health region) in 2000-2004 were DCOs. The percentage of lost to follow-up was 0.7% (1.5% in Donostia health region and 1.2% in Bidasoa) in the first period and 1.4% in the second (3% in Araba health region).

Tabla 2
Five-year relative survival, standardized by age, in patients diagnosed of cancer between 1995 and 2004, by province (a) and health region of residence (b)

	Men		Women	
	1995-1999	2000-2004	1995-1999	2000-2004
a) Provinces				
Araba	43.5 (41.6-45.5)	55.1 (53.3-56.8)	56.1 (53.8-58.3)	60.2 (58.0-62.3)
Gipuzkoa	45.1 (43.9-46.4)	53.1 (51.9-54.2)	58.0 (56.6-59.4)	60.7 (59.4-62.1)
Bizkaia	40.8 (39.9-41.8)	48.5 (47.6-49.4)	55.3 (54.1-56.4)	58.7 (57.6-59.7)
b) Health regions				
Araba*	44.0 (41.9-46.0)	56.2 (54.3-58.1)	56.2 (53.8-58.6)	61.0 (58.7-63.2)
Alto Deba**	43.9 (39.6-48.2)	53.0 (49.3-56.7)	59.3 (54.5-63.9)	58.0 (53.3-62.5)
Bajo Deba**	50.2 (46.5-53.8)	53.4 (50.0-56.7)	61.9 (57.5-66.2)	57.8 (53.5-62.0)
Donostia**	46.4 (44.0-48.8)	52.5 (50.3-54.7)	57.8 (55.3-60.3)	61.3 (58.8-63.7)
Bidasoa**	44.5 (40.6-48.4)	55.4 (51.8-58.9)	58.6 (54.1-62.8)	62.1 (57.9-66.0)
Gipuzkoa**	41.8 (39.1-44.4)	52.7 (50.3-55.1)	55.1 (51.9-58.1)	59.8 (56.8-62.6)
Goierri**	45.4 (42.0-48.9)	49.8 (46.5-53.0)	57.8 (53.5-61.9)	62.6 (58.7-66.3)
Tolosa**	45.9 (41.4-50.4)	57.7 (53.5-61.7)	60.7 (55.6-65.6)	64.8 (59.7-69.6)
Interior***	40.8 (38.8-42.7)	45.9 (44.0-47.7)	54.3 (51.9-56.6)	58.6 (56.4-60.7)
Portugalete-Enkarterri***	41.3 (38.9-43.7)	46.8 (44.5-49.0)	55.3 (52.3-58.2)	59.4 (56.6-62.1)
Barakaldo-Sestao***	37.9 (35.4-40.5)	45.7 (43.3-48.2)	56.0 (52.7-59.1)	56.7 (53.6-59.7)
Uribe***	42.1 (39.6-44.7)	49.2 (46.8-51.5)	55.4 (52.5-58.3)	58.4 (55.7-60.9)
Bilbo***	40.8 (39.2-42.5)	51.4 (49.8-52.9)	55.5 (53.6-57.4)	58.9 (57.1-60.6)

*Health regions corresponding to the Araba province **Health regions corresponding to the Gipuzkoa province
***Health regions corresponding to the Bizkaia province

Table 3
Relative excess risk (RER) of death at five years in patients diagnosed with cancer between 1995 and 2004, by provinces (a) and health regions of residence (b)

	Model 1		Model 2	
	RER (IC95%)	p	RER (IC95%)	p
a) Analysis by provinces				
Sex				
Hombres	1.00 (reference)	0.000	1.00 (reference)	0.000
Mujeres	0.74 (0.73-0.76)		0.92 (0.90-0.94)	
Date of diagnosis				
1995-1999	1.00 (reference)	0.000	1.00 (reference)	0.000
2000-2004	0.84 (0.82-0.85)		0.88 (0.86-0.90)	
Provinces				
Araba	1.00 (referencia)		1.00 (referencia)	
Gipuzkoa	0.99 (0.96-1.03)	0.704	0.99 (0.96-1.03)	0.741
Bizkaia	1.11 (1.08-1.15)	0.000	1.06 (1.03-1.09)	0.000
b) Analysis by health regions				
Sex				
Men	1.00 (reference)	0.000	1.00 (reference)	0.000
Women	0.74 (0.73-0.76)		0.95 (0.93-0.97)	
Date of diagnosis				
1995-1999	1.00 (reference)	0.000	1.00 (reference)	0.000
2000-2004	0.84 (0.82-0.85)		0.89 (0.88-0.91)	
Health regions				
Araba*	1.00 (reference)		1.00 (reference)	
Alto Deba**	1.02 (0.95-1.09)	0.558	0.97 (0.91-1.04)	0.377
Bajo Deba**	0.96 (0.90-1.02)	0.168	0.98 (0.92-1.04)	0.453
Donostia**	1.02 (0.97-1.06)	0.472	1.03 (0.99-1.08)	0.147
Bidasoa**	0.94 (0.88-1.01)	0.072	0.97 (0.91-1.03)	0.311
Gipuzkoa**	1.07 (1.02-1.13)	0.003	1.03 (0.98-1.08)	0.318
Goierri**	1.04 (0.98-1.11)	0.173	1.04 (0.98-1.11)	0.151
Tolosa**	0.91 (0.84-0.98)	0.009	0.97 (0.90-1.04)	0.42
Interior***	1.16 (1.11-1.21)	0.000	1.08 (1.03-1.12)	0.001
Portugalete-Enkarterri***	1.15 (1.10-1.20)	0.000	1.06 (1.01-1.11)	0.015
Barakaldo-Sestao***	1.20 (1.15-1.26)	0.000	1.11 (1.06-1.17)	0.000
Uribe***	1.13 (1.08-1.18)	0.000	1.04 (0.99-1.09)	0.098
Bilbo***	1.10 (1.06-1.14)	0.000	1.08 (1.04-1.12)	0.000

Model 1: standardized by age and adjusted for sex and date of diagnosis.
Model 2: standardized by age and adjusted for sex. date of diagnosis and case-mix.
*Health region corresponding to the Araba province
**Health regions corresponding to the Gipuzkoa province
***Health regions corresponding to the Bizkaia province
CI: confidence interval

A worse RS at 5 years were observed in Bizkaia province, in both sexes and period studied (table 2). Barakaldo-Sestao health region in men showed a lower RS in both periods whereas in women corresponded to Interior and Barakaldo-Sestao health regions in the first and second period, respectively. Table 3 shows the results of the multivariate analysis, with the estimates of relative excess risk of death at five years by provinces and health regions of residence. RER of death was lower in women and in the period 2000-2004 than in men and also in the period 1995-1999 both by province and health region. Cancer patients living in Bizkaia had a significantly higher RER compared to the province of reference in the two models considered (RER1=1.11; CI95%: 1.08-1.15 and RER2=1.06; CI95%: 1.03-1.09). We observed a higher risk of death in all health regions in Bizkaia in the first model and in all of them except Uribe in the second one. In contrast, for the province of Gipuzkoa, we only found statistically significant differences in model 1 in the Gipuzkoa and Tolosa health regions (RER= 1.07; CI95%: 1.02-1.13 and RER= 0.91; CI95%: 0.84-0.98, respectively).

DISCUSSION

Five-year relative survival was lower in Bizkaia both in men and women. In addition, Bizkaia showed a significantly higher excess of risk compared to Araba province in all health regions with the exception of Uribe. In the Gipuzkoa province we only observed statistically significant differences in Gipuzkoa and Tolosa health regions, and these did not remain significant after adjusting for potential confounders. The fact that the Tolosa health region was found to have a significantly lower RER than the health region of reference (Araba), may be due to data on cancer cases with poor prognosis being less complete for Tolosa (confirmed by the DCO percentage), as it has a private hospital (which has a management agreement with the public health service) and not all the sources of information usually used in public hospitals were available for this institution. However, the results obtained in Bizkaia are not related with worse completeness and/or validity of the information. On the other hand, our study indicates longer survival in women than in men and an increase in survival rates over time, and these patterns are in agreement with data published on cancer in the Basque Country[3].

The European project EUROCARE[2,4], with data from population-based cancer registries across Europe, including the Basque Country, stands out as among the most important research that studies between-country differences in cancer survival. Recently, differences in survival between countries have been observed to decrease with respect to previous periods[2]. In Spain, in various types of cancer, differences in survival have been detected between regions[5] and even within the same region[3]. To the best of our knowledge, the present study is the first to analyse cancer survival in the various health regions within the Basque Country, therefore it is not possible to make comparisons with similar studies. On the other hand, it is important to highlight that differences in survival found in our study decreased after adjusting for the case-mix, a pattern which has been reported previously[7].

This study uses data from a population-based registry, that of the Basque Country, that collects information on cases in accordance with international criteria and shows good data-quality indicators in all the study area, characteristics which strengthen the validity of the results. Another strength of the study is that the effects of competing causes of death were controlled for by the estimation of the RS. However, despite cancer survival being influenced by the stage of the disease at diagnosis, this information was not routi-

nely collected during the study period by the BCR.

To conclude, as a measure, overall RER can give us an idea of the effectiveness of management of cancer patients in our region, regardless of the patient sex, age, date of diagnosis and case-mix, and allowed us to identify the lower five-year survival in Bizkaia, not only at province level, but also in their health regions. The causes of these differences should be investigated in more detail and in specific cancer locations in order to develop new policies and strategies to improve cancer control and care in the Basque Country.

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