PERGAMON

European Journal of Cancer 38 (2002) 574–577

European Journal of Cancer

www.ejconline.com

Incidence of breast cancer on Crete, 1994–1995

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Received 11 July 2001; received in revised form 29 October 2001; accepted 15 November 2001

Abstract

The aim of this study was to present epidemiological results relating to malignant neoplasms of breast using primary data from the island of Crete, Greece, 1994–1995. The patients were all female residents of Crete with breast cancer first diagnosed during 1994 and 1995, 208 and 207 new incident cases, respectively. The data were collected and analysed by the Cancer Registry of Crete (CRC). Direct age-standardised rates (ASR) for incidence and cumulative risk (to age 75 years) were calculated for Crete as a whole. Standardised incidence ratios (SIR) were calculated for the 20 provinces (administrative regions); these were also smoothed using Bayesian methods. The ASR for incidence per 100 000 person-years was 70.6. The truncated rate (age 40 years and above) was 153.7. The SIR for the 20 provinces showed no marked variations, with three exceptions, two of which had ratios higher than 1 and one lower. Bayesian smoothing of provincial incidence rates showed that throughout Crete, the risk of breast cancer shows considerable uniformity. The incidence rate of breast cancer on Crete is higher than that of Greece overall, and is comparable with other southern European countries. A possible explanation is that the published incidence for Greece may be an underestimation of the true rate. The small variability in breast cancer incidence within Crete probably reflects the homogeneity of the population and environmental and social conditions.

Keywords: Descriptive epidemiology; Incidence; Breast cancer; Cancer registration; Small area variability

1. Introduction

This report discusses epidemiological results relating to breast cancer on Crete, the largest Greek island (8331.23 km^2), shown in Fig. 1, with a population of 536 980 (census 1991). Socio-economic conditions on Crete, diet and smoking habits have been reviewed in [1]. Cancer mortality for 1992–1993 has also been reported previously [1].

Mortality rates are available for all southern European Union (EU) countries, but not incidence rates. Only estimated incidence rates [2–5] exist, based on empirical relationships (regression models) between incidence and mortality. These relationships involve model parameters, which are estimated using data from selected regional cancer registries in which both mortality and incidence are known. These estimated parameters are then applied to the national mortality data. Obviously the quality of the estimated incidence depends on the existence of such registries, the extent of the covered population, the quality of the collected registration data and the inter-country comparability of the mortality data.

The estimated age standardised rates (ASR) for incidence per 100 000 women for breast cancer in 1996 in the EU [6] were as follows:

NET	DEN	FRA	BEL	SWE	FIN	UK	GER	IRE	AUS	ITA	POR	SPA	GRE
121.7	114.2	108.3	108.1	107.0	105.0	98.1	96.2	95.7	89.3	85.0	72.8	63.5	63.3

The rates for southern EU countries (Greece, Spain, Portugal and Italy) were the lowest; the ratio between the highest and lowest rates, The Netherlands and Greece, respectively, is almost 2-fold. The reasons for these differences between countries are difficult to explain. The quality of the estimation procedure must play a role, and there are grounds to believe that it underestimates incidence in southern EU countries. For example, the incidence rates above, for the EU Mediterranean countries [6], were based on nine regional registries in France, 14 in Italy, and nine in Spain, which covered only relatively small proportions of the total population. Greece and Portugal were not represented by any such regional registries; instead incidence rates

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0959-8049/02/$ - see front matter
PII: S0959-8049(01)00401-4

for these two countries were estimated using registries from Italy and Spain.

Information on cancer incidence is critical for many purposes, including the planning of prevention strategies, monitoring use and management of health services, evaluation of treatments and interventions, and research in the role of environmental carcinogenic factors. Such information should be based on data which are complete, accurate, validated by sound methods of ascertainment and analysed by appropriate statistical methods. Furthermore, many of the above purposes require accurate information not only at national level, but also for small areas. The motivation for this report is 2-fold: (a) to publish up-to-date information on cancer incidence on Crete based on primary data collected by local registration; and (b) to present, for the first time in Greece, information on the small-area variation of risk for breast cancer.

2. Patients and methods

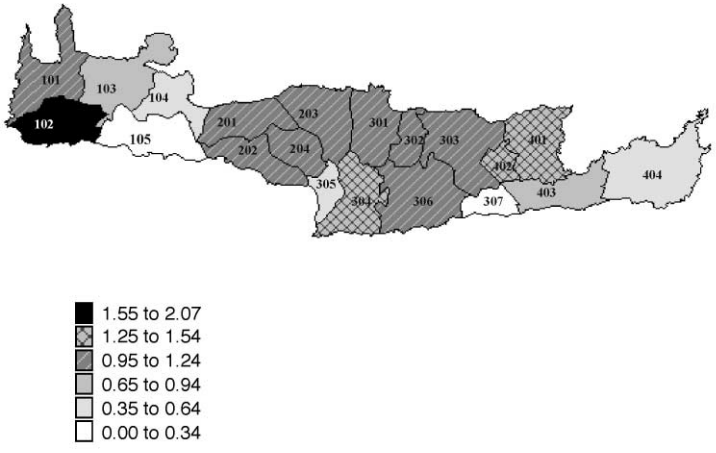
This report discusses results pertaining to breast cancer incidence in 1994 and 1995, the third and fourth year of the population-based Cancer Registry of Crete (CRC), Greece. In Greece there is no mandatory case reporting, nor is there a national or local health information network. On Crete the data are therefore collected by the CRC from all hospitals, pathology laboratories and other related sources, as well as notifications from death registries; more details on data sources and methods of collection and quality control have been published in Ref. [1].

The patients were all female residents of Crete with breast cancer who were first diagnosed during 1994 or 1995. There were 208 and 207 new incident cases, respectively. The information stored in the CRC database for every case includes personal identity details, age, sex, place of residence, occupation, Health Insurance Fund, histology of tumour, date of diagnosis, date and cause of death. Grade of tumour and treatment modality are recorded only if related information is available. The International Classification of Diseases (ICD-9) is used to classify incidence cases from histology reports; pathology diagnoses are coded according to morphological groupings.

For the geographical variation (according to place of residence) of relative risk, small-area was defined as 'province' (second level administrative regions). There are 20 provinces in Crete, within four 'prefectures' (first level). The names and number-codes of the provinces are shown in Fig. 1 and the number-codes in Table 1: provinces 101–105 belong to the prefecture of Chania, 201–204 to Rethymnon, 301–307 to Heraklion and 401–404 to Lassithi.

2.1. Statistical analysis

To calculate the age-standardised rate (ASR) for incidence, the female population of Crete was divided into 5-year age spans in accordance with the 1991 Greek Census. The ASR and truncated ASR (for age 40 years and above) per 100 000 person-years were calculated by direct standardisation, using the European Standard Population [7]. The cumulative risk for ages up to and including 75 years was also calculated [8]. Ninety-five percent Confidence Intervals (95% CI) were computed using the exact binomial variance [8]. Area-specific relative risks, for age 40 years and above (392 women



No.	Province
101	Kissamos
102	Selino
103	Kydonia
104	Apokoronas
105	Sfakia
201	Rethymnon
202	Ag. Vassilios
203	Mylopotamos
204	Amari
301	Malevizi
302	Temenos
303	Pediada
304	Kenoyrgio
305	Pyrgiotissa
306	Monofatsi
307	Viannos
401	Merabello
402	Lassithi
403	Ierapetra
404	Sitia

Fig. 1. Standardised incidence ratios (SIR) of breast cancer for Cretan women (aged 40 years and above), 1994–1995.

(94.5%) (Table 2), for the 20 provinces were estimated by the standardised incidence ratios (SIR); their 95% CI were estimated using tables of the Poisson distribution [9,10]. To allow for the extra-Poisson variation, known to exist for rare diseases and small areas, two further estimates were calculated. Both were based on three-stage hierarchical Bayesian formulations of the three underlying density functions: for the number of incident cases, the risks and the parameters of the density of the latter [11,12]. The chosen models were Poisson-Gamma-Gamma (P/G/G) and Poisson-Normal-Conditional Autoregression (P/N/CAR) [11–14]. The first is appropriate for modelling population risk and leads to estimates which have optimum robustness properties [15,16], while the second allows also any spatial patterns in disease to be taken into account; i.e. when geographically close areas tend to have similar disease rates [11–14]. It is for this reason that the second model (P/N/CAR) yields estimates, which are often shrunk more towards the mean. The two models were implemented by Markov Chain Monte Carlo methods [11,17], using the Bayesian inference using Gibbs sampling (BUGS) code [18]. For each model, 1000 'burn-in' samples were followed by a 'production' run of 10 000 samples (single chain); estimates of the SIR were obtained by the posterior means and precision was assessed by the 95% Bayesian credible intervals.

3. Results

In 1994 and 1995, the CRC recorded 415 new incident female cases with malignant neoplasm of the breast. Table 2 shows the age distribution of incident cases and the corresponding age-specific incidence rates. The ASR for breast cancer was 70.6 new cases per 100 000 person-years (95% CI: 64.1, 77.1). The truncated ASR (age 40 years and above) was 153.7 (95% CI: 137.8, 169.6) and the cumulative risk (ages 0–75 years) was 5.7% (95% CI: 5.1, 6.4).

Table 1 shows the estimates of the area-specific relative risks (for age 40 years and above) for each of the 20 provinces of Crete as yielded by the three methods of statistical estimation. The classical SIRs (shown also in Fig. 1) are maximum likelihood estimates and, as expected, vary widely around their mean of 0.99 (standard deviation (S.D.) = 0.46). Ignoring known limitations associated with P values of tests comparing SIRs with unity, there are three provinces with marked or significant results, provinces 102 (marked), 103 and 401 (significant). The relative risks of the first and third are larger than one, while that of the second is lower than one. However, with 20 such tests the significance level should be lowered to account for the inflation in the probability of the type I error. This would be equivalent to increasing the width of the confidence interval; so

Table 1
Estimates of standardised incidence ratios (SIR) of breast cancer for Cretan women (aged 40 years and above), 1994–1995 by provinces[a]

Province code	Person-years	No. of incident cases		SIR and 95% CI		Bayesian (P/G/G) estimate of SIR and 95% credible interval		Bayesian (P/N/CAR) estimate of SIR and 95% credible interval	
		Observed	Expected						
101	4356	16	14.34	1.12	0.64, 1.81	1.11	0.67, 1.66	1.10	0.70, 1.62
102	1468	10	4.83	2.07	0.99, 3.80	1.71	0.91, 2.80	1.38	0.79, 2.27
103	20 480	48	67.41	0.71	0.53, 0.94	0.73	0.54, 0.94	0.77	0.59, 0.98
104	2623	5	8.63	0.57	0.19, 1.35	0.70	0.30, 1.28	0.81	0.48, 1.22
105	478	0	1.57	0.00	0.00, 3.69	0.69	0.11, 1.71	0.91	0.51, 1.42
201	8277	32	27.60	1.16	0.79, 1.64	1.15	0.81, 1.57	1.11	0.81, 1.48
202	1918	7	6.40	1.09	0.44, 2.26	1.09	0.51, 1.87	1.01	0.64, 1.49
203	4119	17	13.73	1.24	0.72, 1.98	1.21	0.74, 1.80	1.18	0.81, 1.64
204	1250	5	4.17	1.21	0.39, 2.80	1.15	0.50, 2.10	1.13	0.70, 1.73
301	4755	17	15.26	1.11	0.65, 1.78	1.11	0.67, 1.64	1.11	0.77, 1.54
302	29 459	102	94.53	1.08	0.89, 1.31	1.08	0.89, 1.30	1.08	0.88, 1.34
303	8021	28	25.74	1.09	0.72, 1.57	1.09	0.74, 1.50	1.09	0.79, 1.45
304	4614	21	14.81	1.42	0.88, 2.17	1.37	0.88, 1.97	1.25	0.88, 1.73
305	2345	4	7.53	0.53	0.14, 1.36	0.68	0.27, 1.27	0.93	0.57, 1.37
306	5834	18	18.72	0.96	0.57, 1.52	0.98	0.61, 1.44	1.02	0.71, 1.39
307	1178	1	3.78	0.26	0.01, 1.47	0.61	0.15, 1.35	0.85	0.46, 1.35
401	6246	31	20.91	1.48	1.01, 2.10	1.43	0.99, 1.95	1.30	0.92, 1.78
402	1142	5	3.82	1.31	0.42, 3.05	1.21	0.52, 2.23	1.10	0.64, 1.76
403	5278	13	17.67	0.74	0.39, 1.26	0.78	0.44, 1.21	0.84	0.55, 1.20
404	5777	12	19.35	0.62	0.32, 1.08	0.68	0.38, 1.07	0.74	0.46, 1.10

95% CI, 95% Confidence Interval.

[a] Bayesian estimates based on Poisson-Gamma-Gamma (P/G/G) formulation and Poisson-Normal-Conditional Autoregression (P/N/CAR) formulation.

Table 2
Number of incident cases of breast cancer on Crete (1994–1995) by age, and age-specific rates (ASR) per 100 000 person-years

Age (years)	Cases *n*	ASR
0–24	0	0
25–29	2	5.5
30–34	11	30.9
35–39	10	31.0
40–44	25	78.5
45–49	35	133.8
50–54	47	152.6
55–59	42	137.3
60–64	62	191.9
65–74	100	209.8
75–84	62	190.2
85+	19	217.2

using instead the 99% CI, for province 102 that is (0.77, 4.43), for 103 (0.48, 1.02) and for 401 (0.89, 2.32). Thus, only province 103 has perhaps a markedly lower relative risk of breast cancer. In contrast, the Bayesian methods have produced much more homogeneous estimates of the relative risks, reflected in the small standard deviations of 0.30 and 0.18, for the P/G/G and P/N/CAR models, respectively. They both agreed that only provinces 103 and 401 have 95% credible intervals not or marginally including unity, respectively. Again similar considerations as before would consider the result for province 103 as 'marked', but 'not significant'.

4. Discussion

The ASR for incidence of breast cancer (70.6; 95% CI: 64.1, 77.1) was significantly higher in Crete than the estimate of 63.3 for the total Greek population. One explanation might be that the incidence for Greece [6] was underestimated because of the methods used. The rate for Crete is similar to those of Italy and Spain, both of which had provided incidence data used in the estimation methods [6].

Evidence-based assessment of health-related issues (risks, services, etc.) requires accurate incidence rates not only at the national level, but also for small areas. This is indeed one of the purposes and advantages of regional population-based cancer registration. Estimates of small-area risks have never been made in Greece. In this study, the small-area distribution of the relative risk for breast cancer (for women, aged 40 years and above) was measured at the level of province according to the place of residence. Relative risks were estimated by three methods, which produced similar results. The differences between the 20 provinces were small. For the three exceptions, indicated by the classical SIR, two were of weak significance, which was lowered by Bayesian methods, while the third remained marked, but also non-significant. Thus, throughout Crete, the risk of breast cancer shows good uniformity, reflecting the homogeneity of the population and the similarity of the prevailing environmental and social conditions.

Acknowledgements

This work received partial support in the form of grants by the Europe Against Cancer Programme (1993) of the EU, and by the Regional Operational Programmes of Crete (1994–1999) of the EU (Framework II).

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