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Original Paper

Improvement in Survival of Patients with Cancer of the Kidney in Europe

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Survival of adult patients with cancer of the kidney, renal pelvis, ureter and urethra (ICD-9 189) was analysed using data from the EUROCARE II study, a collaborative project of 45 population-based cancer registries in 17 European countries. For the period 1985–1989, more than 24 000 patients were included and 5-year relative survival was 48%. Large variations were observed between countries with 5-year relative survival ranging from 57% in France, 53% in Italy and 51% in Spain to 35% in Denmark, 33% in Poland and 30% in Estonia. A number of registries also provided information on previous years and survival was seen to improve with time from 44% in 1978–1980 to 50% in 1987–1989. Age was an important determinant of survival with 5 year survival rates decreasing from 63% in patients aged 15–44 years to 36% in patients aged 75 years and older. Variation in survival rates by country or time is probably related to differences in the distribution of tumour stage at diagnosis. Evidence to confirm this theory is, however, lacking. © **1998 Elsevier Science Ltd. All rights reserved.**

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INTRODUCTION

In 1995 the first monograph on survival of cancer patients in Europe was released showing huge variation between countries [1]. The collaborative EUROCARE project has now been extended to 45 cancer registries in 17 countries and to a more recent time period. From this project we will report on the results regarding cancer of the kidney in adults.

In many epidemiological studies, cancer of the renal parenchyma is analysed together with cancer of the renal pelvis and the ureter. However, clinical studies tend to distinguish between urothelial carcinoma and renal cell carcinoma, being separate clinical and aetiological entities. Urothelial carcinoma of ureter and renal pelvis are generally presented to the clinician as a result of haematuria. Diagnosis is ascertained by pyelography or endoscopy and treatment consists of nephroureterectomy when the extent of invasion in surrounding tissues is limited. As for bladder cancer [2], differentiation between invasive and non-invasive urothelial tumours may be difficult.

Renal cell carcinoma can be diagnosed after macroscopic haematuria but systemic complaints such as fatigue and weight loss can also be the presenting symptom. Treatment consists of nephrectomy when the tumour is still localised. Response to other types of treatment is poor. In recent decades, diagnosis is increasingly made incidentally by modern imaging techniques such as computer tomography scan and ultrasonography, often performed for non-related complaints [3, 4]. These incidental tumours are generally small and have a good prognosis [3, 4]. Benign renal tumours are frequently found at autopsy and distinction between these adenomas and small carcinomas can be complicated [5].

PATIENTS AND METHODS

This study presents results from the EUROCARE II database which contains data for more than 24 000 patients with cancer of the kidney, renal pelvis, ureter and urethra, diagnosed in 15 European countries (Table 1). Survival data were collected by 45 population-based cancer registries and a minimum follow-up of 5 years was required. Less than 0.3% of patients were lost to follow-up. Cases discovered at

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Table 1. *Coverage with cancer registries and number of adult cases by country for kidney cancer (EUROCARE* II*)*

Country	% Coverage of registries	No. of cases included 1985–1989
Northern Europe		
Finland	100	2605
Sweden*	17	835
Denmark	100	2847
U.K.		
Scotland	100	2002
England	50	7696
Western and Central Europe		
The Netherlands*	6	336
Germany*	2	555
Switzerland*	11	362
France*	6	597
Southern Europe		
Spain*	10	765
Italy*	10	2324
Eastern Europe		
Slovenia	100	507
Slovakia	100	1706
Poland*	6	634
Estonia	100	580
Europe	–	24 351

* < 20% of the national population covered. Countries with only a small number of cases are not shown.

Table 2. *Subsite distribution and proportion histologically verified by country for adult kidney cancer (EUROCARE* II*)*

	% Kidney	% Pelvis/ ureter/ urethra	% Other/ nos	% HV
Northern Europe				
Finland	92	7	1	93
Sweden*	78	15	7	95
Denmark	76	23	1	91
U.K.				
Scotland	84	14	2	77
England	85	13	2	71
Western and Central Europe				
The Netherlands*	78	21	1	91
Germany*	90	7	3	91
Switzerland*	78	22	0	100
France*	88	10	2	92
Southern Europe				
Spain*	68	13	19	88
Italy*	86	12	2	77
Eastern Europe				
Slovenia	90	9	1	88
Slovakia	91	9	0	76
Poland*	96	3	1	67
Estonia	95	5	0	78

HV, histologically verified. * < 20% of the national population covered. Countries with only a small number of cases are not shown.

autopsy, patients first diagnosed with another tumour or known on the basis of a death certificate only were excluded, as were cancers diagnosed in children. Results from the Austrian and Icelandic registry are not presented because of small numbers.

As some countries are represented by regional registries, general European estimates were calculated using a weighted analysis, taking into account the annual number of incident cases. Relative survival was computed as the ratio between the observed (crude) survival and the expected survival, derived from general mortality data [6]. To control for differences in age distribution between countries, relative survival was calculated using age-standardised estimates. Cancer of the kidney was more common in men with a male–female ratio of 3:2. Survival data were combined for both sexes because the survival rates appeared to be similar.

The ICD-9 category 189 comprises several distinct histological entities and subsites. Urothelial carcinomas are mainly found in the renal pelvis (ICD-9 189.1) or the ureter (ICD-9 189.2) whereas renal cell carcinomas, formerly referred to as hypernephroma or Grawitz tumour, arise from the renal parenchyma (ICD-9 189.0). Nephroblastoma, also referred to as Wilms' tumour, occur in children, but were excluded from this study. Other invasive histotypes exist but are relatively rare as are tumours of the urethra and the para-urethral gland (ICD-9 189.3–189.4). Analogous to mortality statistics, survival data were not separated by histotype or subsite which hampers comparison with clinical series. A number of population-based studies have demonstrated that patients with urothelial carcinoma have a better prognosis than those with renal-cell carcinoma [7, 8]. Direct comparison of survival rates between countries may be biased as a result of the variation in the distribution by subsite (Table 2). The proportion of tumours of renal pelvis, ureter and urethra ranged from 23% in Denmark and 22% in Switzerland to 5% in Estonia and 3% in Poland. Stratified analysis should have improved comparisons but the validity of the information on subsite was insufficient for some countries.

Not all registries have access to clinical information and urothelial tumours may be erroneously classified as ICD 189.0 (kidney not otherwise specified). In Spain, unspecified cases were classified as 189.9. As a result, it is unknown to what extent the observed variation in subsite distribution is related to incidence patterns, definition of disease or registration practice. The aetiologies of renal cell carcinoma and urothelial carcinoma are assumed to be different albeit both histotypes have been related to tobacco smoking. This explains the male preponderance of kidney cancer but geographical incidence patterns clearly differ from other smoking-related cancers.

RESULTS

Intercountry variation in survival

Figure 1 shows that 5-year relative survival varied from 57% in France to 30% in Estonia. Survival rates were also relatively poor in Poland (33%), Denmark (35%) and Scotland (36%). Good results were seen for Italy (53%) and Spain (51%). Large variation was also observed within individual countries, for example in Italy, Spain and France (data not shown), although the confidence intervals were quite wide.

Time trends and the effect of age on survival

5 year survival improved considerably from 44% in 1978–1980 to 50% in 1987–1989 (Table 3). Both observed and relative survival decreased with age, with 5-year relative survival decreasing from 63% for patients younger than 45 years

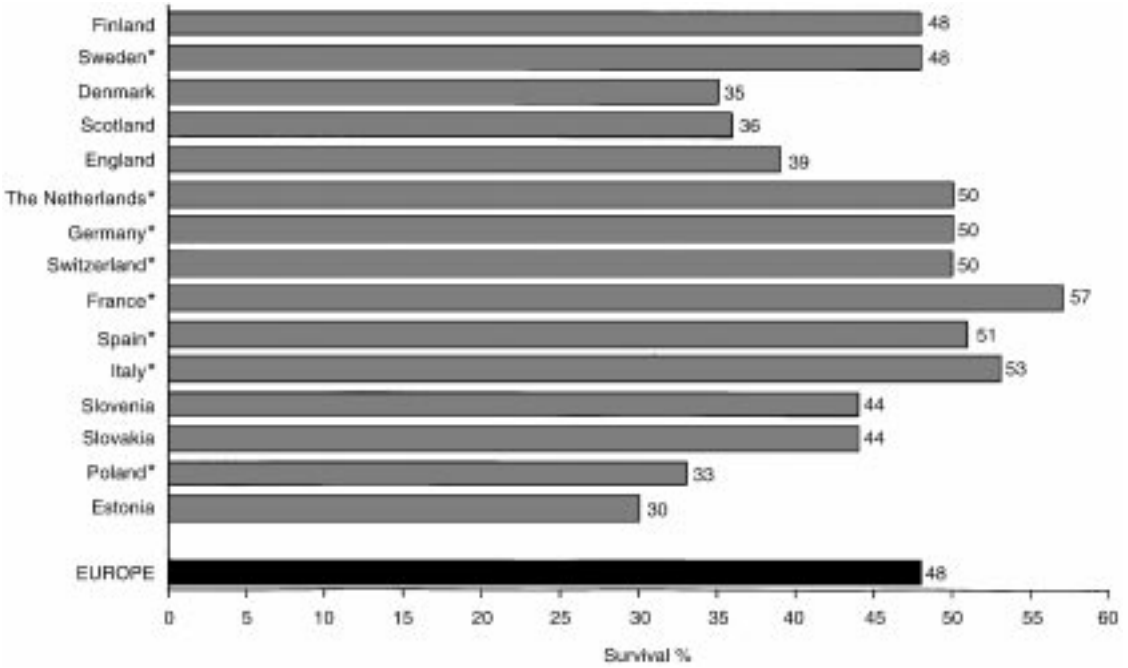

Figure 1. Relative 5-year survival rates (age-standardised) for adult patients with cancer of the kidney, both sexes, 1985–1989 (EUROCARE II). * < 20% of the national population covered.

of age to 36% for those over 74 years (Table 4). This difference in survival was evident after only one year, with survival rates of 82% and 53% for patients aged 15–54 and 75 and over, respectively.

DISCUSSION

This study demonstrates considerable variation in survival for kidney cancer within Europe, despite existing uniformity in treatment guidelines. Apart from methodological issues discussed elsewhere [9, 10], the main explanation for this variation is inequality in the distribution of stage at diagnosis.

Table 3. *Change in* 1-, 3- *and* 5-*year relative survival over time for adult patients, both sexes, with kidney cancer (EUROCARE* II*)*

	1978–1980	1981–1983	1984–1986	1987–1989
1 year	62	64	66	68
3 year	48	52	52	54
5 year	44	46	47	50

Table 4. *One and* 5-*year observed and relative survival by age for* 1985–1989, *adult patients, both sexes, with kidney cancer (EUROCARE* II*)*

	Age group				
	15–44	45–54	55–64	65–74	75–99
1-year					
Observed	82	77	72	63	48
Relative	82	77	73	65	53
5-year					
Observed	63	57	49	37	21
Relative	63	59	53	45	36

As long as the tumour is limited to the kidney, surgical treatment may offer a good chance of cure [11], independent of tumour size [12]. For advanced tumours, however, results are generally poor, even with additional systemic treatment [11, 12]. A favourable stage distribution is associated with the availability of diagnostic facilities for people with urological complaints and with the frequency of incidental diagnosis through modern imaging methods [3, 4]. The potential for early detection is corroborated by the high prevalence of renal cancer at autopsy [13], which also raises the issue of tumours with a low malignant potential. To what extent these tumours are included in cancer registry files is difficult to estimate without detailed studies.

Theoretically, variation in the distribution by histotype or subsite could influence survival comparisons. Histotype distributions may influence results as survival has been shown to be better for urothelial carcinoma. In Denmark, 5-year crude survival for urothelial carcinoma was 38% in men and 31% in women against 25 and 28% for renal cell carcinoma [7]. In the U.S.A., 5-year relative survival for urothelial carcinoma was 66% for men and 57% for women compared with 58 and 59% for renal-cell carcinoma [8]. These American figures clearly exceed the 48% 5-year relative survival observed in Europe. Clinical series report even better results but in these studies advanced tumours, elderly patients or tumours not histologically verified are generally excluded. Table 2 showed that 5% (Sweden) to 33% (Poland) of tumours were not microscopically verified, suggesting that the extent of disease or the physical condition of the patients made them unsuitable for diagnosis or treatment. For some registries histological information is not always available, leading to underestimation of the proportion of microscopically verified cases. For the countries in Eastern Europe, the low proportions are probably real and reflect the lack of medical facilities. Coexistence of Balkan endemic nephropathy [14] might also interfere with treatment opportunities.

Despite the absence of important progress in treatment options, survival rates improved with time which should be attributed to the improving availability of modern diagnostic facilities in most countries. For Italy, Spain and France large variation was observed between the individual registries. For these countries, survival rates also appeared to be better than had been expected on the basis of the mortality/incidence ratios on a national level [15]. This may suggest that health-care facilities are better in regions covered by cancer registries and that the results from these registries are not representative for the entire country.

Poor survival in the elderly is the subject of debate. A few studies have reported stage distribution to be comparable with that for younger patients and suggested that minor differences in resection rates or postoperative mortality could not explain the variation in survival [16, 17]. However, elderly patients with localised cancer experience worse survival, suggesting that tumour behaviour is more aggressive at a later age. A major study from the U.S.A. [11] contradicts these findings and suggests that survival rates are particularly worse for advanced tumours. Given the increasing proportion of elderly patients, the issue of age-related survival differences certainly requires further study.

For the future, early diagnosis of tumours of the kidney by active case finding should be encouraged and especially repeated haematuria calls for further examination. Introduction of screening programmes is intriguingly attractive but would have a poor cost–benefit ratio because the actuarial lifetime risk is only 0.5%. The low specificity of current diagnostic methods would cause a large number of false positive results. Development of effective systemic treatment would have a greater impact than screening but, unfortunately, progress is still pending.

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APPENDIX

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