

A wide difference in cancer survival between middle aged and elderly patients in Europe

Alberto Quaglia^{1*}, Riccardo Capocaccia², Andrea Micheli³, Eugenio Carrani², Marina Vercelli^{1,4} and the EUROCARE-3 Working Group[†]

¹Liguria Region Cancer Registry at the Descriptive Epidemiology Unit, National Cancer Research Institute, Genoa, Italy

²National Center of Epidemiology, Surveillance and Promotion of Health, National Institute of Health, Rome, Italy

³Descriptive Epidemiology and Public Health Planning Unit, National Cancer Institute, Milan, Italy

⁴Department of Health Sciences, University of Genoa, Italy

Nowadays the burden of cancer in elderly people has reached an alarming extent. The purpose of this study is comparing cumulative and conditional relative survival in elderly patients between 65 and 84 years and younger adults aged from 55 to 64. Fifty-three cancer registries of 22 European countries, participating in the EUROCARE-3 programme, collected information on the cases diagnosed over the period 1990–1994. We computed cumulative and conditional relative survival for 16 cancer sites. Middle aged patients experienced a better prognosis than the elderly for all cancer sites, in both sexes and the differences were more marked at 1 than 5 years since diagnosis. The very large differences noted in the first period after cancer detection declined in the subsequent years and, when 5-years conditional survival was considered, for several cancers the elderly and younger adults had the same probabilities of surviving. The death relative excess risks (RERs) in the elderly with respect younger individuals were really very high and markedly larger at 1 than 5 years, and in women than men. Genitourinary and gynaecological cancers showed the highest RERs, around 2.0 and between 1.5 and 2.5 respectively. This very high early mortality could be due not only to clinical aspects: the barriers to health care access and a consequent late diagnosis might represent for elderly patients the main determinant of this very large prognostic disadvantage. In conclusion, clinical management of cancer in the elderly remains a major issue to be faced with complex social and health care policies.

© 2007 Wiley-Liss, Inc.

Key words: cancer; conditional and cumulative relative survival; health care inequalities; elderly

Western populations are rapidly ageing; this phenomenon has accelerated at least since the early 80 s. Now the magnitude of this issue has reached an alarming extent and the burden of chronic diseases like cancer requires an extraordinary effort by health care systems and social services.

According to data by the United Nations, in 2000 the elderly over 65 years amounted in Northern, Western and Southern Europe to about 13–14% and 18–19% of all resident population in men and in women respectively. The phenomenon will reach a peak when the people born during the period of the “baby boom”, in the 50–60 s, will be 65 years old. For instance, in Italy, the country with the highest proportion of people aged 65 years or over (15% in men and 21% in women), by 2030 this population segment will represent 29% and 35% of total population.¹

In this demographic context the cancer burden is quickly increasing; on one hand incidence and mortality trends of some major cancers are levelling off or declining, on the other hand crude rates are growing as a consequence of people ageing.²

If we consider the single European macro-regions in 2002, we observe very variant situations: in Eastern countries only 49% in men and 48% in women of all cancers were detected in the elderly, the corresponding values increased to 67% and 58% in Northern Europe, while they were slightly lower in Southern (63% and 56%) and in Western countries (60% and 56%). As regards mortality, the registered deaths from cancer in the elderly were 52% and 60% in Eastern Europe, 74% and 73% in Northern, 70%

and 73% in Southern, 69% and 75% in Western for men and women respectively.³

Despite of these demographic and epidemiological figures and the greater attention of oncologists and geriatricians, clinical management of cancer in the elderly remains a major issue.⁴

Actually, large population-based studies on cancer survival in Europe found marked differences between the elderly and middle aged individuals.^{5,6} The prognosis observed for European elderly cancer patients was very poor if compared with that of the same age patients from the U.S.; in Europe, unlike the U.S., cancer survival depended strongly on age at diagnosis.⁷

The present study, an in depth analysis of EUROCARE-3 programme,⁸ is aimed at describing relative survival rates of cancer patients aged from 65 to 84 years in 22 European countries, by providing an update of data referred to the last available incidence period (1990–1994). The investigation is focused on the prognostic differences between the elderly and the younger adults (55–64 years).

Material and methods

The elderly from 65 to 84 years and middle aged adults from 55 to 64 years, diagnosed during the period 1990–1994, were considered for the analysis. People aged 85 or more years were not included because of the limits inherent the statistics in the very elderly, namely the poorer completeness and quality of data collection.^{6,9} Table I shows the number of cases for the two age groups, by sex and every country participating in EUROCARE 3 study, while in Table II the same number of cases is displayed by cancer site. Elderly patients were 435,319 in men and 347,886 in women, while 148,103 and 150,280 in middle aged subjects.

The information on incident cases was collected by 53 cancer registries (CRs) of 22 European nations: namely Denmark, Estonia, Finland, Iceland, Malta, Norway, Slovakia, Slovenia, Scotland, Sweden and Wales whose populations were covered completely by national registries; Austria, Czech Republic, England, France, Germany, Italy, Poland, Portugal, Spain, Switzerland and The Netherlands where there was only a partial monitoring by local regional CRs.

Department to which the work should be attributed: SSD Descriptive epidemiology, Liguria Cancer Registry, National Cancer Research Institute, Genoa, Italy.

Grant sponsor: EUROCARE-3, BIOMED-2 ; Grant number: BMH4-CT98-3390; Grant sponsor: the Compagnia di San Paolo, Torino, Italy.

*Correspondence to: Alberto Quaglia, SSD Descriptive epidemiology-Liguria Cancer Registry, National Cancer Research Institute, Largo Rosanna, Benzi 10–16132, Genoa, Italy. Fax: +39-010-560-0956. E-mail: alberto.quaglia@istge.it

Received 20 July 2006; Accepted after revision 31 October 2006

DOI 10.1002/ijc.22515

Published online 6 February 2007 in Wiley InterScience (www.interscience.wiley.com).

TABLE I – NUMBER OF CASES FOR TOTAL CONSIDERED CANCERS, DIAGNOSED DURING THE PERIOD 1990–1994, BY SEX, AGE GROUP AND EUROPEAN COUNTRY (EUROCARE-3)

Country	Number of cases			
	Men		Women	
	55–64 (years)	65–84 (years)	55–64 (years)	65–84 (years)
North				
Denmark	7,249	21,304	9,186	20,858
Finland	6,350	17,716	6,559	14,849
Iceland	285	926	357	607
Norway	5,513	20,604	5,458	15,678
Sweden	10,149	43,956	12,253	32,166
United Kingdom				
England	44,590	159,987	52,139	126,556
Scotland	8,445	25,574	9,552	21,971
Wales	4,278	16,274	5,134	12,986
Centre-West				
Austria	1,049	2,771	870	2,467
France	3,261	6,899	3,130	5,885
Germany	2,434	5,764	1,899	5,819
Switzerland	1,055	13,883	1,012	10,528
The Netherlands	5,619	2,491	4,932	2,279
South				
Italy	19,667	47,802	15,360	35,822
Malta	134	425	181	350
Portugal	425	1,181	1,124	1,264
Spain	7,517	16,294	5,297	10,189
East				
Czech Republic	1,926	3,154	1,352	2,710
Estonia	2,964	3,855	2,344	4,152
Poland	4,405	6,646	3,808	6,506
Slovakia	7,462	12,922	5,623	9,507
Slovenia	3,326	4,891	2,710	4,737
<i>All Countries</i>	<i>148,103</i>	<i>435,319</i>	<i>150,280</i>	<i>347,886</i>

TABLE II – NUMBER OF CASES DIAGNOSED IN ALL PARTICIPATING EUROPEAN COUNTRIES DURING THE PERIOD 1990–1994, BY SEX, AGE GROUP AND CANCER SITE (EUROCARE-3)

Site	Number of cases			
	Men		Women	
	55–64 years	65–84 years	55–64 years	65–84 years
Stomach	11,129	34,401	4,515	21,790
Colon	14,614	44,893	12,418	48,214
Rectum	12,119	31,182	7,103	24,055
Pancreas	5,378	14,261	3,786	16,095
Larynx	6,223	8,874	702	1,311
Lung	45,336	112,482	14,634	42,214
Melanoma	4,395	6,706	4,357	8,346
Breast			60,083	96,099
Cervix			5,181	8,677
Corpus			12,509	21,159
Ovary			10,449	19,093
Prostate	17,768	110,748		
Bladder	16,459	42,455	4,179	13,900
Kidney	7,587	14,491	4,014	10,053
Thyroid	595	954	1,509	2,650
NHL	6,500	13,872	4,841	14,230
<i>Total</i>	<i>148,103</i>	<i>435,319</i>	<i>150,280</i>	<i>347,886</i>

NHL, Non-Hodgkin's lymphoma.

Survival of countries without national registration is represented by the pooled data of participating CRs in that country. The values presented as European survival rates were obtained as the weighted average of the corresponding survival rates in each country. Therefore European survival can be considered as the average survival of all countries taken into account.

The relative survival rates were computed, through the Hakulinen's methods,¹⁰ for the following malignant tumours: stomach, colon, rectum, pancreas, larynx, lung, melanoma, breast, cervix and corpus uteri, ovary, prostate, kidney, bladder, thyroid and non-Hodgkin's lymphoma (NHL).

Age-standardised survival rates (ASSR) were calculated, due to the different distribution of age within the 2 age groups, by the direct method using as standard the distribution of cases by cancer site in the entire EUROCARE-3 database.¹¹

The comparability among countries with different age structure populations and among different age groups of patients was assured by the age-standardisation and the use of relative survival which takes into account the age-specific mortality rates.¹¹

We estimated the conditional survival by dividing the cumulative survival at 5 years from diagnosis by the cumulative survival at 1 year. Conditional survival is the likelihood for an individual to continue to survive for some specified survival duration, up to the condition of having already survived for a certain duration after diagnosis of cancer.¹² Death Relative Excess Risks (RERs), which express the excess mortality, were calculated as the ratio of the relative survival logarithm in the 65–84 age group to that in the 55–64 years, in order to highlight differences in prognosis by age. For all the epidemiological indicators the related Confidence Intervals (CI) at 95% level were also computed on the basis of the standard errors.

Results

Cumulative relative survival

Tables III and IV show the ASSR for the elderly patients (65–84 years) and for the younger adults (55–64 years), by cancer site, at 1 and 5 years after diagnosis, for women and men respectively.

The 1-year survival was lower in the elderly than in the younger age group for all sites. The differences were always statistically significant, except for melanoma in women.

Also the 5-year survival was always higher in younger patients. The differences by age were statistically significant in all sites except for pancreas and thyroid in men.

Conditional relative survival

Conditional survival is presented in the last columns of Tables III and IV, by cancer site and the 2 age groups, in women and men respectively.

The 1-year survival differed greatly between elderly and younger adults, the 5-year survival showed lower differences, but the smallest variations were observed for 5-year conditional survival. The lowest differences, below 5 percentage points, were registered for colon, rectum, larynx and lung in both sexes, for thyroid, melanoma and NHL in men and breast and ovary in women. The largest differences were noted for cervix and corpus uteri (around 12 points), bladder (11 points), stomach (10 points) and kidney (9 points) in women, for bladder and stomach (8 points) in men.

The death RERs of the elderly compared to middle aged patients

Table V shows the excess mortality by means of death RERs in elderly patients aged from 65 to 84 years compared to younger patients from 55 to 64, by sex and cancer site at 1 and 5 years for cumulative relative survival and at 5 years for conditional relative survival after diagnosis.

The RERs of elderly patients were higher for women than for men in all considered cancer sites, both at 1 and 5 years, except lung and bladder cancers at 1 year and lung at 5 years. The RERs at 5 years from diagnosis in men were equal or lower than 1.3 for cancers of colon, rectum, pancreas, larynx, lung, melanoma and thyroid; they were between 1.4 and 1.6 for stomach, prostate, kidney and NHL; only bladder cancer showed a higher RER. The RERs in women were 1.3 for cancers of colon, pancreas and lung; they were between 1.4 and 1.7 for stomach, rectum, larynx, melanoma, breast and ovary. Cervix and corpus uteri, bladder, kidney, thyroid cancers and NHL had values around 2 or more.

The RERs at 1 year were markedly higher than those at 5 years in both sexes, except melanoma in women; in particular, in women the largest decreases of RERs from 1 to 5 years were observed for

TABLE III – ASSR OF FEMALE PATIENTS (DIAGNOSED DURING THE PERIOD 1990–1994) AT 1 AND 5 YEARS AFTER DIAGNOSIS BY AGE GROUP (55–64 AND 65–84 YEARS) AND CANCER SITE. (EUROPEAN POOL, EUROCARE-3)

Site	55–64 years ¹		65–84 years ¹		55–64 years ²		65–84 years ²		Conditional survival ^{3,4}	
	ASSR	(95% CI)	ASSR	(95% CI)	ASSR	(95% CI)	ASSR	(95% CI)	55–64 years	65–84 years
Thyroid	90.5	(88.0–93.2)	61.4	(59.6–63.2)	84.9	(81.6–88.4)	52.2	(50.0–54.5)	93.8	85.0
Melanoma	94.9	(93.3–96.5)	93.0	(92.4–93.7)	85.1	(82.6–87.7)	76.7	(75.4–78.0)	89.7	82.5
Breast	95.2	(94.7–95.6)	87.8	(87.6–88.1)	77.4	(76.6–78.3)	68.5	(68.1–68.8)	81.4	78.0
Corpus Uteri	93.4	(92.4–94.5)	82.6	(82.0–83.2)	83.6	(82.1–85.3)	63.6	(62.8–64.5)	89.5	77.0
Bladder	86.2	(83.5–89.0)	70.7	(70.0–71.5)	75.1	(71.8–78.7)	53.9	(53.0–54.9)	87.2	76.2
Colon	78.6	(77.1–80.1)	64.8	(64.4–65.2)	55.5	(53.6–57.5)	46.3	(45.8–46.8)	70.7	71.5
Larynx	92.7	(90.4–94.9)	76.6	(74.2–79.1)	66.8	(58.3–76.6)	53.8	(50.3–57.5)	72.1	70.2
Kidney	79.5	(77.3–81.7)	58.8	(57.8–59.7)	62.7	(59.7–65.7)	41.1	(40.0–42.2)	78.9	69.9
NHL	80.2	(78.1–82.4)	60.7	(60.0–61.5)	60.4	(57.5–63.3)	40.0	(39.1–40.9)	75.3	65.9
Rectum	83.3	(81.5–85.1)	69.9	(69.3–70.5)	55.0	(52.5–57.6)	43.7	(43.0–44.5)	66.1	62.5
Cervix Uteri	85.8	(84.0–87.7)	68.0	(67.3–69.1)	61.2	(58.5–64.1)	39.7	(38.5–40.9)	71.3	58.4
Stomach	51.6	(48.6–54.8)	35.7	(35.1–36.4)	31.1	(28.2–34.4)	18.1	(17.5–18.7)	60.2	50.7
Ovary	72.5	(70.8–74.4)	47.6	(46.9–48.3)	36.6	(34.6–38.7)	22.0	(21.4–22.7)	50.4	46.2
Lung	35.6	(34.0–37.3)	21.1	(20.7–21.5)	11.5	(10.5–12.8)	6.2	(5.9–6.4)	32.4	29.4
Pancreas	19.3	(16.9–22.0)	12.6	(12.2–13.2)	6.28	(4.7–8.4)	3.0	(2.8–3.4)	32.6	23.8

ASSR, age-standardised survival rates; 95% CI, confidence intervals at 95% level; NHL, Non-Hodgkin's lymphoma.

¹1 year after diagnosis.–²5 year after diagnosis.–³Cancer sites ordered according to the decreasing rank of the conditional survival in the 65–84 age group.–⁴5-years relative survival conditioned on having survived more that 1 year.

TABLE IV – ASSR OF MALE PATIENTS (DIAGNOSED DURING THE PERIOD 1990–1994) AT 1 AND 5 YEARS AFTER DIAGNOSIS BY AGE GROUP (55–64 AND 65–84 YEARS) AND CANCER SITE. (EUROPEAN POOL, EUROCARE-3)

Site	55–64 years ¹		65–84 years ¹		55–64 years ²		65–84 (years) ²		Conditional survival ^{3,4}	
	ASSR	(95% CI)	ASSR	(95% CI)	ASSR	(95% CI)	ASSR	(95% CI)	55–64 years	65–84 years
Thyroid	73.4	(65.5–82.1)	59.9	(56.5–63.4)	57.5	(48.6–67.9)	48.0	(43.5–52.9)	78.3	80.1
Melanoma	92.5	(90.9–94.2)	89.7	(88.7–90.7)	74.4	(71.4–77.5)	69.0	(67.2–71.0)	80.4	76.9
Bladder	91.1	(90.3–91.9)	78.9	(78.4–79.3)	76.5	(75.1–77.9)	60.0	(59.3–60.6)	84.0	76.0
Larynx	87.8	(86.3–89.3)	80.8	(79.7–81.9)	64.4	(62.1–66.8)	58.6	(56.8–60.5)	73.4	72.5
Colon	76.2	(74.9–77.5)	64.3	(63.8–64.7)	52.6	(50.8–54.3)	45.5	(44.9–46.1)	69.0	70.8
Kidney	76.1	(74.3–77.9)	59.1	(58.2–60.0)	58.2	(55.8–60.6)	41.4	(40.3–42.6)	76.4	70.1
Prostate	92.7	(92.0–93.4)	85.1	(84.9–85.4)	69.1	(67.6–70.6)	58.1	(57.6–58.5)	74.5	68.3
NHL	76.6	(74.6–78.7)	58.1	(57.2–59.0)	51.7	(49.1–54.4)	36.7	(35.6–37.8)	67.5	63.2
Rectum	80.7	(79.3–82.1)	68.2	(67.6–68.7)	49.4	(47.6–51.4)	41.1	(40.4–41.9)	61.3	60.3
Stomach	46.1	(44.4–47.8)	31.8	(31.3–32.3)	23.8	(22.3–25.5)	14.1	(13.7–14.6)	51.7	44.3
Lung	36.7	(35.8–37.5)	22.8	(22.6–23.1)	12.0	(11.4–12.6)	6.4	(6.2–6.6)	32.7	28.1
Pancreas	17.7	(15.8–19.8)	11.8	(11.3–12.3)	3.3	(2.6–4.2)	3.1	(2.8–3.5)	18.7	26.3

ASSR, Age standardised survival rates; 95% CI, confidence intervals at 95% level; NHL, Non-Hodgkin's lymphoma.

¹1-year after diagnosis.–²5-year after diagnosis.–³Cancer sites ordered according to the decreasing rank of the conditional survival in the 55–64 and 65–84 age group.–⁴5-year relative survival conditioned on having survived more that 1 year.

TABLE V – RELATIVE EXCESS RISKS OF DEATH (RERS) OF 65-84 VERSUS 55-64 AGE GROUP AT 1 AND 5 YEARS AFTER DIAGNOSIS FOR CRS AND CONDITIONAL RELATIVE SURVIVAL, BY SEX AND CANCER SITE (EUROPEAN POOL, EUROCARE-3)

Site	Women				Men				Women		Men	
	1 year (CRS)		5 years (CRS)		1 year (CRS)		5 years (CRS)		5-year Conditional survival		5-year Conditional survival	
	RERs	(95% CI)	RERs	(95% CI)	RERs	(95% CI)	RERs	(95% CI)	RERs	(95% CI)	RERs	(95% CI)
Stomach	1.6	(1.5–1.7)	1.5	(1.4–1.6)	1.5	(1.4–1.5)	1.4	(1.3–1.4)	1.3	(1.3–1.4)	1.2	(1.2–1.3)
Colon	1.8	(1.7–1.9)	1.3	(1.3–1.4)	1.6	(1.6–1.7)	1.2	(1.2–1.3)	1.0	(0.9–1.0)	0.9	(0.9–1.0)
Rectum	2.0	(1.8–2.2)	1.4	(1.3–1.5)	1.8	(1.7–1.9)	1.3	(1.2–1.3)	1.1	(1.1–1.2)	1.0	(1.0–1.1)
Pancreas	1.3	(1.2–1.3)	1.3	(1.2–1.4)	1.2	(1.2–1.3)	1.0	(1.0–1.1)	1.3	(1.2–1.4)	0.8	(0.8–0.8)
Larynx	3.5	(3.0–4.5)	1.5	(1.3–2.1)	1.6	(1.5–1.8)	1.2	(1.2–1.3)	1.1	(0.9–1.5)	1.0	(1.0–1.0)
Lung	1.5	(1.5–1.6)	1.3	(1.3–1.3)	1.5	(1.5–1.5)	1.3	(1.3–1.3)	1.1	(1.1–1.1)	1.1	(1.1–1.2)
Melanoma	1.4	(1.2–1.8)	1.7	(1.5–1.9)	1.4	(1.3–1.6)	1.3	(1.2–1.3)	1.8	(1.7–1.9)	1.2	(1.2–1.3)
Breast	2.6	(2.4–2.8)	1.5	(1.4–1.5)					1.2	(1.2–1.2)		
Cervix Uteri	2.5	(2.3–2.8)	1.9	(1.8–2.0)					1.6	(1.5–1.7)		
Corpus Uteri	2.8	(2.5–3.2)	2.5	(2.4–2.8)					2.4	(2.2–2.5)		
Ovary	2.3	(2.2–2.5)	1.5	(1.5–1.6)					1.1	(1.1–1.2)		
Prostate					2.1	(2.0–2.3)	1.5	(1.4–1.5)			1.3	(1.3–1.3)
Bladder	2.3	(2.0–2.9)	2.2	(1.9–2.5)	2.5	(2.4–2.7)	1.9	(1.8–2.0)	2.0	(1.8–2.1)	1.6	(1.5–1.6)
Kidney	2.3	(2.1–2.6)	1.9	(1.8–2.1)	1.9	(1.8–2.1)	1.6	(1.6–1.7)	1.5	(1.4–1.6)	1.3	(1.3–1.4)
Thyroid	4.9	(4.0–6.5)	4.0	(3.4–4.9)	1.7	(1.4–2.3)	1.3	(1.2–1.7)	2.5	(2.3–2.8)	0.9	(0.9–1.0)
NHL	2.3	(2.1–2.5)	1.8	(1.7–2.0)	2.0	(1.9–2.2)	1.5	(1.5–1.6)	1.5	(1.4–1.6)	1.2	(1.1–1.2)

CRS, Cumulative relative survival; 95% CI, confidence intervals at 95% level; NHL, Non-Hodgkin's lymphoma.

cancers of colon (1.8–1.3), rectum (2.0–1.4), larynx (3.5–1.5), breast (2.6–1.5), cervix (2.5–1.9), ovary (2.3–1.5) and thyroid (4.9–4.0); in men the differences were weaker: the widest ones were observed for rectum (1.8–1.3), bladder (2.5–1.9) and prostate

cancers (2.1–1.5). The RERs obtained from conditional survival were in agreement with that seen in the previous paragraph 3.2. As already shown in Tables III and IV, the conditional survival at 5 years improved largely the probability of surviving the first year

after diagnosis; this was confirmed by the conditional RERs which were generally lower than the cumulative RERs at 1 year.

Discussion

Differences in survival between the elderly and middle aged adults

Survival rates of elderly patients were always lower than those of younger adults. This is a clear evidence already highlighted in the previous reports of the EUROCARE programme.^{5,6} In the present updating the age-related differences would seem to be even larger than those registered in the past. However, such a comparison is not completely reliable because data here presented refer to a higher number of European populations now included in the study.¹¹ Another article, in preparation, will deal with the differences in survival trend by age showing more comparable data.

Nevertheless, the observed RERs for patients diagnosed during the period 1990–1994 appeared to be very high, and very marked differences in prognosis were observed. For breast, urological and gynaecological cancers, elderly women experienced an excess mortality at 5 years from diagnosis increased by 100% compared to younger subjects, and elderly men had risks higher than 50% for urological cancers and NHL.

The data were also analysed for each country to look for geographical variations of survival differences by age. However we did not observe major geographical variability and no country usually showed more or less marked differences in prognosis between elderly and younger adults.

It is reasonable to believe that the big efforts made by oncologists and geriatricians in the last 15 years to optimise the clinical management of senior patients had not yet achieved the expected results in the mid 90 s.⁴ There is much evidence that the percentage of cancer patients treated with potentially definitive and curative therapies diminishes with age increase.^{13–15}

Chronological advanced age represents a risk factor for under-treatment, even after adjustment for markers of physical frailty, comorbidity and social support.^{16,17} At present the elderly are still less likely to be referred to clinical trials, owing to the use of chronological age as the only enrolment criterion; that could be the cause of a certain lack of appropriate protocols and evidence-based data on side effects of clinical treatments.^{18,19}

It is difficult to assess if the under-treatment is a correct choice, influenced by physiologic impairment and pathologic condition of the elderly, or if an intensive approach could become an excessive risk of over-treatment.

Notwithstanding these uncertainties, now many physicians have understood that the elderly patients need a multidimensional evaluation which takes into account several factors affecting clinical decisions. By means of the comprehensive geriatric assessment it is possible to select the frail old patients and the aged persons with a good physical condition who can benefit from a standard treatment applied to younger people.²⁰

On virtue of a more careful evaluation of presented data, 3 major results are worth discussing. Firstly the very different survival pattern according to the duration after diagnosis, secondly the different behaviour of prognosis according to sex and finally the role played by the anatomical site to determine a particular prognosis in the senior patients.

Differences in survival by age: The role of duration after diagnosis and the marked impact of the first year

It is noteworthy that the elderly experienced a different prognostic disadvantage according to the time since diagnosis. We computed RERs at 1 and 5 years from diagnosis just to highlight variations in the relative risk of death during the follow-up. The differences between the older and the younger cohorts were more marked at 1 than 5 years in nearly all cancer sites. Indeed, most of excess mortality by age was confined to the first year after diagnosis, particularly for women.

Conditional survival, that is the probability of surviving 5 years conditioned on having survived more than 1 year, is an epidemiological index seldom used in scientific publications. In the present analysis it was applied essentially to underline the strong effect of the period after diagnosis in determining survival differences between younger and older patients. Most of the very large 1-year prognostic disadvantage in the elderly reduced considering 5-year conditional survival and in many cases the differences disappeared.

A part of elderly patients died within the first year and this group should represent the frailest subjects, suffering deeply from surgical mortality, the toxicity of the first therapies and the advanced stage at presentation. The elderly who survived this critical period were probably selected by a biological and clinical point of view (perhaps tumours slowly growing or with favourable prognostic factors) and their survival from the second to the fifth year is better than that of younger adults. As a consequence, the older person who survived the first year seemed to have a prognosis similar to the younger one.

This very high early mortality could be due to different aspects, not only of clinical nature. First of all the barriers to health care access and a consequent late diagnosis might represent for elderly patients the main determinant of this very large prognostic disadvantage. This fact is confirmed by some studies reporting a more advanced stage at presentation in older patients.^{13,21,22} In this respect it is worthy to remind the differences in survival existing between the elderly in Europe and the U.S.: the large gap in Europe is not observed in the U.S. and this seems to be due to the reduced difference in this latter country in the disease stage between the 2 age groups.⁷

Senior patients are more likely to suffer from comorbidity and, in some percentage, they are frail also because of the physiological impairment.²³ The frailty increases the mortality and morbidity related to surgery, radiotherapy and chemotherapy, and limits the use of aggressive and potentially curative treatment. The older patients in a good health condition and with a localised disease extension, who can undergo the same conventional therapies as younger individuals, have nearly the same chances to survive as middle aged adults.

Differences in survival by age: The role of sex

Generally, women have a better cancer survival than men. This fact is often explained by a higher attention to their own body and a greater awareness of health care issues, even though a possible role played by biological differences cannot be disregarded.²⁴

However, we found that RERs of elderly women were always higher than those of elderly men. It would seem that the prognostic advantage of women over men before 65 years partially declines in a subsequent time. Probably in the elderly we have to take into account other aspects which might reduce the general tendency, and make the differences between younger and older women greater than those between younger and older men.

Recent studies have found very high correlations between elderly cancer survival and socio-economic factors, health care resources and some demographic indicators (marital status and household composition).^{25,26} This social effect was particularly notable in elderly women, more often widows and living alone, with a low income and a low educational level. A poor socio-economic and emotional support could play a relevant role by affecting a timely and easy access to health care.

Differences in survival by age: The role of cancer site

Genitourinary and gynaecological cancers showed the highest RERs. The poor prognosis of the latter could be related both to a difficult access to health care and the substantial lack of screening best-suited for older people. Also a delay in seeking medical consulting may be an additional cause, due to a lower awareness of the cancer issue and a greater sense of decency for a cohort of women born before 1930.

The consequence is a late stage at diagnosis and a high early mortality, as showed by the 1-year RERs registered for breast (2.6) and cervical (2.5) cancers. There is no evidence to stop the screening at a specific age and to exclude the elderly from early detection programmes solely on the basis of age "per se". Actually older persons represent a heterogeneous group of people with very different characteristics and screening after 60 years should be based on life expectancy and a multidimensional evaluation.²⁷

However, it has to be taken into account that not always a successful screening programme for cervical cancer is characterised by a resulting improved survival in old women, even if the elderly have a higher incidence than screened women.^{28,29}

These results are confirmed by a large population-based study which found that age was associated to a more advanced extension disease at diagnosis for women but not men and particularly for ovary, cervix and corpus uteri cancers.³⁰ There are other reports claiming that gynaecological cancers continue to represent a significant problem in the elderly.^{22,31}

As regards genitourinary tumours, the much poorer prognosis of older patients could be due to an inverse significant relationship of stage to age, and the complexity of surgical procedures as well as the particular physiological role of kidney. In addition, both bladder and kidney cancers have cigarette smoking as common etiologic factor and patients suffering from these tumours are often affected also by comorbid conditions, such as cardiovascular and pulmonary diseases which can mask the cancer symptoms and delay, or in some way vary, the time of diagnosis.³²

The very high RERs observed for NHL are in agreement with the main clinical reports recently published: the rates of complete remission diminish quickly with age giving rise to a consequent low survival; many patients with intermediate- and high-grade NHL do not receive an appropriate therapy because of age alone; however, the lymphoid malignancies have a more aggressive behaviour in older people.³³ On the other hand, the increased incidence of serious infections following myelotoxicity caused by heavy chemotherapeutic regimens has also to be taken into account. Protocols specifically tailor-made for concomitant diseases must be developed by randomised clinical trials in order to overcome this issue.³³

The final comment concerns the poor prognosis for thyroid cancer in the elderly, probably caused by a different histological type distribution according to age: a more aggressive anaplastic histology is more frequent in the older persons, while at younger age and especially in women the papillary subtype, which has a very good prognosis, is very common.

Four main conclusions emerge from this analysis: firstly the prognosis in the elderly was largely poorer than that of younger adults; the survival advantage commonly observed in women with respect men was less notable in elderly people: older women had risks of dying much higher than older men; even if survival pattern is common for almost all the malignancies, the disadvantage of the elderly was more evident for some specific cancer sites; finally, the elderly patients who survived the first period after diagnosis experienced a prognosis similar to that of younger individuals as highlighted by the conditional survival data.

Deepened studies, aimed at finding the reasons for the high mortality in the first period after detection, are needed. It is important to adopt new evaluation methods, like the comprehensive geriatric assessment. The purpose should be the selection of old patients with a good physical status to be submitted to the same standard protocols as younger ones and benefit from the same aggressive therapies, as well as to improve modified clinical strategies to adapt to frail elderly.

Acknowledgements

†The EURO CARE-3 Working Group: Austria–W Oberaigner (Tyrol Cancer Registry, Innsbruck). Denmark–H H Storm (Danish Cancer Society, Department of Cancer Prevention and Documentation, Copenhagen). Estonia–T Aareleid (Estonian Cancer Registry,

Tallinn). Czech Republic–M Jechova, M Rousarova (IHIS and West Bohemia Cancer Registry, Prague). Finland–T Hakulinen (Finnish Cancer Registry, Helsinki). France–G Hédelin (Bas-Rhin Cancer Registry, Strasbourg); G Launoy (Calvados Digestive Cancer Registry, Caen); J Macé-Lesec'h (Calvados General Cancer Registry, Caen); J Faivre (Côte d'Or Digestive Cancer Registry, Dijon); G Chaplain (Côte d'Or Gynaecologic Cancer Registry, Dijon); P-M Carli (Côte d'Or Malignant Haemopathies Registry, Dijon); A Danzon (Doubs Cancer Registry, Besancon); B Tretarre (Hérault Cancer Registry, Montpellier); M Colonna (Isère Cancer Registry, Meylan); B Lacour (Lorraine Childhood Cancer Registry, Nancy); N Raverdy (Somme Cancer Registry, Amiens); C Berger and B Freycon (Rhône-Alpes Childhood Registry, Saint-Etienne); P Grosclaude (Tarn Cancer Registry, Albi); and J Estève (University of Lyon, Lyon). Germany–H Ziegler (Saarland Cancer Registry, Saarbrücken); and D Hölzel and G Schubert Fritschle (Munich Cancer Registry, Munich). Iceland–L Tryggvadottir (Icelandic Cancer Registry, Reykjavik). Italy–F Berrino (Project Leader), C Allemani, P Baili, L Ciccolallo, P Crosignani, G Gatta, A Micheli, M Sant, E Taussig, S Sowe (Istituto Nazionale per lo Studio e la Cura dei Tumori, Lombardy Cancer Registry, Milan); S Ferretti (Ferrara Cancer Registry, Ferrara); V. Ramazzotti, MC Cercato (Latina Cancer Registry, Rome); M Vercelli and M.A. Orengo (Liguria Region Cancer Registry, DISSAL University GE, IST Genova, Genova); F Pannelli, S. Vitarelli (Macerata Cancer Registry, Marche Childhood Cancer Registry, Camerino); M Federico and ME Artioli (Modena Cancer Registry, Modena); M Ponz De Leon and P Benatti (Modena Colorectal Cancer Registry, Modena); V De Lisi and L Serventi (Parma Cancer Registry, Parma); R Zanetti and S Patriarca (Piedmont Cancer Registry, Turin); L Gafà and R Tumino (Ragusa Cancer Registry, Ragusa); F Falcini (Romagna Cancer Registry, Forli); M Budroni (Sassari Cancer Registry, Sassari); E Paci and E Crocetti (Tuscan Cancer Registry, Firenze); P Zambon, S Guzzinati (Venetian Cancer Registry, Padova); and R Capocaccia, E Carrani, R De Angelis, P Roazzi, M Santaquilani, A Tavilla, F Valente, and A Verdecchia (Istituto Superiore di Sanità Rome); Malta–M Dalmas (Malta National Cancer Registry, Valletta); Norway–F Langmark and A Andersen (Cancer Registry of Norway, Institute of Population-based Cancer Research, Oslo). Portugal–P Pinheiro (Southern Portugal Cancer Registry, Lisbon); Poland–J Rachtan (Krakow Cancer Registry, Krakow) and M Bielska-Lasota, Z Wronkowski, and M Zwierko (Warsaw Cancer Registry, Warsaw). Slovakia–I Pleško and A Obsitníhová (National Cancer Registry of Slovakia, Bratislava). Slovenia–V Pompe-Kirm and M Primic-Zakelj (Cancer Registry of Slovenia, Ljubljana). Spain–I Izarzugaza (Basque Country Cancer Registry, Vitoria-Gasteiz); C Martinez-Garcia (Granada Cancer Registry, Granada); I Garau (Mallorca Cancer Registry, Palma de Mallorca); C Navarro and M D Chirlaque (Murcia Cancer Registry, Murcia); E Ardanaz and C Moreno (Navarra Cancer Registry, Pamplona, Navarra); J Galceran (Tarragona Cancer Registry, Reus). Sweden–L Barlow (Cancer Registry of Sweden, Stockholm), and T Möller (Southern Swedish Regional Tumour Registry, Lund University Hospital, Lund). Switzerland–G Jundt (Basel Cancer Registry, Basel); and J M Lutz and C Bouchardy (Geneva Cancer Registry, Geneva). The Netherlands–J W W Coebergh (Eindhoven Cancer Registry, Eindhoven) and O Visser (Amsterdam Cancer Registry, Amsterdam). UK–S Godward (East Anglian Cancer Registry, Cambridge); M P Coleman (London School of Hygiene and Tropical Medicine, London); E M I Williams (Merseyside and Cheshire Cancer Registry, Liverpool); D Forman (Northern and Yorkshire Cancer Registry and Information Service, Leeds); M J Quinn (Office for National Statistics, London); M Roche and S Edwards (Oxford Cancer Intelligence Unit, Oxford); J Verne (South West Cancer Intelligence Services, Bristol); H Møller and J Bell (Thames Cancer Registry, London); H Botha, (Trent Cancer Registry, Sheffield); G Lawrence (West Midlands Cancer Intelligence Unit, Birmingham); R Black (Scottish Cancer Intelligence Unit, Edinburgh); and J A Steward (Welsh Cancer Intelligence and Surveillance Unit, Wales).

References

- United Nations Population Division. World population Prospects: The 2000 Revision.
- De Flora S, Quaglia A, Bencicelli C, Vercelli M. The epidemiological revolution of the 20th century. *FASEB J* 2005;19:892-7.
- Ferlay J, Bray F, Pisani P, Parkin DM. GLOBOCAN 2002 cancer incidence, mortality and prevalence worldwide, Version 2.0. Lyon: IARC Press, 2004. CancerBase No. 5.
- Monfardini S. Geriatric oncology: a new subspecialty. *J Clin Oncol* 2004;186:4655.
- Vercelli M, Quaglia A, Casella C, Parodi S, Capocaccia R, Martinez Garcia C, The EURO-CARE Working Group. Relative survival in elderly cancer patients in Europe. *Eur J Cancer* 1998;34:2264-70.
- Vercelli M, Capocaccia R, Quaglia A, Casella C, Puppo A, Coebergh JWW, The EURO-CARE Working Group. Relative survival in elderly European cancer patients: evidence for health care inequalities. *Crit Rev Oncol Hematol* 2000;35:161-79.
- Gatta G, Capocaccia R, Coleman MP, Ries LAG, Hakulinen T, Micheli A, Sant M, Verdecchia A, Berrino F. Toward a comparison of survival in American and European cancer patients. *Cancer* 2000;89:893-900.
- Berrino F, Capocaccia R, Coleman MP, Estève J, Gatta G, Hakulinen T, Micheli A, Sant M, Verdecchia A, eds. Survival of cancer patients in Europe: the EURO-CARE study. *Ann Oncol* 2003;14Suppl 5:1-155.
- Bain MRS, Harvey JC, Muir CS. Epidemiology research in ageing: perspectives and limitations. In: Balducci L, Lyman GH, Ershler WB, eds. *Geriatric oncology*. Amsterdam: Harwood Academic, 1998.105-114.
- Hakulinen T, Abeywickrama KH. A computer program package for relative survival analysis. *Comp Prog Biomed* 1985;19:197-207.
- Capocaccia R, Gatta G, Roazzi P, Carrani E, Santaquilani M, De Angelis R, Tavilla A, the EURO-CARE Working Group. The EURO-CARE-3 data base: methodology of data collection, standardisation quality control and statistical analysis. In: Berrino F, Capocaccia R, Coleman MP, Estève J, Gatta G, Hakulinen T, Micheli A, Sant M, Verdecchia A, eds. *Survival of cancer patients in Europe: the EURO-CARE study*. *Ann Oncol* 2003;14:14-27.
- <http://seer.cancer.gov/seerstat>
- Bouchardy C, Rapiti E, Fioretta G, Laissue P, Neyroud-Caspar I, Schafer P, Kurtz J, Sappino AP, Vlastos G. Undertreatment strongly decreases prognosis of breast cancer in elderly women. *J Clin Oncol* 2003;21:3580-7.
- Fentiman IS. Are the elderly receiving appropriate therapy for cancer? *Ann Oncol* 1996;7:657-8.
- Muss HB, Longo DL. Cancer in the elderly. *Semin Oncol* 2004;31:125-7.
- Janssen-Heijnen MLG, Smulders S, Lemmens VEPP, Smeenk FWJM, van Geffen HJAA, Coebergh JWW. Effect of comorbidity on the treatment and prognosis of elderly patients with non-small cell lung cancer. *Thorax* 2004;59:602-7.
- Goodwin JS, Hunt WC, Samet JM. Determinants of cancer therapy in elderly patients. *Cancer* 1993;72:594-601.
- Monfardini S, Repetto L, Audisio R, et al. (eds). Guidelines for the management of cancer in the elderly. *Crit Rev Oncol Hematol* 1998;27:85-168.
- Hutchins LF, Unger JM, Crowley JJ, Coltman CA, Albain KS. Underrepresentation of patients 65 years of age or older in cancer-treatment trials. *N Engl J Med* 1999;341:2061-7.
- Repetto L, Fratino L, Audisio RA, Venturino A, Gianni W, Vercelli M, Parodi S, Dal Lago D, Gioia F, Monfardini S, Aapro MS, Serraino Det al. Comprehensive geriatric assessment adds information to ECOG performance status in elderly cancer patients: an Italian group for geriatric oncology study. *J Clin Oncol* 2002;20:494-502.
- Clark PE, Stein JP, Groshen SG, Cal J, Miranda G, Lieskovsky G, Skinner DG. Radical cystectomy in the elderly. Comparison of survival between younger and older patients. *Cancer* 2005;103:546-52.
- Wright JD, Gibb RK, Geevarghese S, Powell MA, Herzog TJ, Mutch DG, Grigsby PW, Gao F, Trinkaus KM, Rader JS. Cervical carcinoma in the elderly. An analysis of patterns of care and outcome. *Cancer* 2005;103:85-91.
- Coebergh JWW, Janssen-Heijnen MLG, Post PN, Razenberg PPA. Serious co-morbidity among unselected cancers patients newly diagnosed in the Southeastern part of The Netherlands in 1993-1996. *J Clin Epidemiol* 1999;52:1131-1136.
- Micheli A, Mariotto A, Giorgi Rossi A, Gatta G, Muti P, the EURO-CARE Working Group. The prognostic role of gender in survival of adult cancer patients. *Eur J Cancer* 1998;34:2271-78.
- Vercelli M, Lillini R, Capocaccia R, Micheli A, Coebergh JW, Quinn M, Martinez-Garcia C, Quaglia A, the ELDCARE Working Group. Is cancer survival in the elderly influenced by socio-economic factors and health care system features? *Eur J Cancer* 2006;42:234-42.
- Quaglia A, Vercelli M, Lillini R, Mugno E, Coebergh JW, Quinn M, Martinez-Garcia C, Capocaccia R, Micheli A, the ELDCARE Working Group. Socio-economic factors and health care system characteristics related to cancer survival in the elderly. A population-based analysis in sixteen European countries (ELDCARE project). *Crit Rev Oncol Hematol* 2005;54:117-28.
- Walter LC, Lewis CL, Barton MB. Screening for colorectal, breast, and cervical cancer in the elderly: a review of the evidence. *Am J Med* 2005;118:1078-86.
- Brenner H, Hakulinen T. Up-to-date long-term survival curves of patients with cancer by period analysis. *J Clin Oncol* 2002;20:826-32.
- Mandelblatt J, Gopaul I, Wistreich M. Gynaecological cancer of elderly women: another look at papanicolaou smear testing. *JAMA* 1986;256:367-371.
- Kant AK, Glover C, Horm J, Schatzkin A, Harris TB. Does cancer survival differ for older patients? *Cancer* 1992;70:2734-40.
- Ferrante JM, Gonzalez EC, Roetzheim RG, Pal N, Woodard L. Clinical and demographic predictors of late-stage cervical cancer. *Arch Fam Med* 2000;9:439-45.
- Raghavan D, Skinner E. Genitourinary cancer in the elderly. *Semin Oncol* 2004;31:249-63.
- Westin EH, Longo DL. Lymphoma e myeloma in older patients. *Semin Oncol* 2004;31:198-05.