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Management and survival of colorectal cancer in the elderly in population-based studies

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ABSTRACT

Colorectal cancer is a major problem in elderly patients. Most data on the management and survival of colorectal cancer has been provided by specialised hospital units and as such cannot be used as reference because of unavoidable selection bias. Cancer registries recording data on treatment and survival at a population level represent the best valuable resource to assess the management of patients. However, there is a paucity of reports published in the literature due to the difficulty to routinely collect such data. Relative survival rates in the elderly were lower than in younger patients. However, the gap that has separated younger from elderly patients is closing. Stage at diagnosis remains the major determinant of prognosis. There is also large variation in survival within countries: survival rates being dramatically lower in Eastern European countries, compared to Western European countries. Comorbidity, which is particularly frequent in the elderly, increases the complexity of cancer management and affects survival. Substantial improvement in the care of colorectal cancer in the elderly has been achieved (increase in the proportion of patients resected for cure, decrease in operative mortality, improvement in stage at diagnosis). Surgery should not be restricted on the basis of age alone. Further improvements can be made, in particular with respect to adjuvant therapy.

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1. Introduction

Colorectal cancer is predominantly a problem of the elderly: 30 to 40% of the cases occur in subjects aged 75 or older.¹ The ageing of the population and the rise in life expectancy, as well as the increasing incidence of colorectal cancer, have led to a growing number of affected patients. Over the past 25 years important advances have occurred in the management of colorectal cancer.² However, diffusion of treatment that has proven beneficial among elderly patients is not well known. Most data on management and survival of colorectal cancer in the elderly is provided by specialised hospital units and as such cannot be used as reference because of unavoidable selection bias. Furthermore, crude survival rates overes-

timate cancer-specific mortality among elderly patients since mortality due to other causes is high. Relative survival, defined as the ratio of observed survival to expected survival in a population of the same age and sex distribution, provides an estimation of patient survival which is corrected for non-colorectal cancer cause of death.³ Population-based studies, recording all cases diagnosed in a well-defined population, represent the best way to assess improvements in management or prognosis of colorectal cancer in the elderly (defined in this paper as patients aged 75 years or older). Such studies are rare, because they require accurate and detailed data collection, which is difficult to achieve for many cancer registries. The purpose of this report is to describe colorectal cancer management and survival in the elderly

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and to explore the factors involved using community-based statistics.

2. Surgery for colorectal cancer

Colorectal cancer is managed by surgical resection of the primary tumour whenever possible. This is the only possibility for cure of the cancer, with the exception of endoscopic polypectomy of a malignant adenoma, which by itself can be a sufficient treatment. A review of 28 independent studies, involving a total of 34,194 patients, has reported a lower resection rate in elderly patients compared to younger patients⁴ (Table 1). This difference between age groups is multifactorial. It may be because of later presentation, poor performance status, presence of comorbidities or an expectation of poorer outcome in elderly patients. However, the gap between age groups is closing. Recent data suggest that the resection rate for colon cancer is now similar in all age groups up until 85 and becomes lower only in the very old age group.^{4,5} The age-related decreased resection rate appears earlier among patients with rectal cancer, just after the age of 80.⁵ This can be explained by the fact that rectal surgery is generally more complex. Several reports from France indicate that there was a major improvement in the proportion of resected cases until the 1990s, after which it levelled out.^{2,6,7} A similar trend has also been reported in Denmark.⁸ The absence of a recent improvement in the proportion of resected cases can be related to the fact that it is not far from the optimum: 90% for colon cancer and 85% for rectal cancer up until 85 years of age.⁵ The observed trend shows a change in the habits and opinions of surgeons and anaesthetists over the years. It is now well established that the quality of surgery is of particular importance in rectal cancer. Total mesorectal excision decreases local recurrence. However, it has been shown that total mesorectal excision was performed less often in elderly patients than in younger patients.⁹ This treatment must be recommended whatever the age. The importance of appropriate treatment does not diminish with age. Age in itself should not be a limiting factor in the treatment of patients with colorectal cancer. A comprehensive geriatric assessment for determining operative risk should assist in selection of patients who otherwise appear unlikely to benefit from surgery.

It is important to underline that the increase in the proportion of patients resected from their cancer is associated with an improvement in the stage at diagnosis.¹⁰ Several explanations can be put forward: earlier consultation, more frequent

and more rapid referral for investigations by general practitioners, a more forceful attitude of surgeons and also, because among non-resected cases in the past, there were patients with early-stage disease which are now identified as such.

The objectives of surgery in elderly patients are to improve life expectancy with a minimal risk of operative mortality and loss of autonomy. A Canadian study compared quality of life of patients over 80 years old who had undergone surgery for colorectal cancer, with a younger group composed of patients under 70.¹¹ Patients were surveyed by mail using the EORTC quality-of-life scales specific to cancer (EORTC – C30) and colorectal cancer (EORTC – CR38). The two groups scored similarly except for physical functioning and stoma-related problems. Most patients did not require special assistance or alternative living arrangements after discharge from the hospital and were able to return to their preoperative level of functioning. This study suggests that elderly patients who are selected for surgery have a quality of life comparable to younger patients in most respects. It is well established that elderly patients have an increased frequency, compared with younger patients, of comorbid conditions such as diabetes, hypertension, chronic obstructive pulmonary disease or cardiovascular and cerebrovascular disease.^{9,12} In a population-based study in the Netherlands the proportion of patients with comorbidity varied from almost 40% in patients aged 50–64 years to more than 70% in those aged 80 years or older.⁹ However, the proportion of patients undergoing surgery was not affected by comorbidity. Elderly patients constitute a heterogeneous group. Post-operative morbidity increases progressively with age, as well as the duration of hospital stay. An increasing frequency of thrombo-embolism, respiratory and cardiovascular complications was reported in relation to age.⁹ Some comorbid conditions at the time of diagnosis predict complications after surgery. This is particularly the case of chronic obstructive pulmonary disease and deep-vein thrombosis.¹³ However, anastomotic leak rates were unchanged.

Available population-based data indicate that the outcomes of surgery, even in the oldest age groups, can be good. It can be concluded that if an elderly patient is believed to be fit for surgery, then a standard surgical procedure with primary anastomosis can be tolerated without excessive risk of surgical complications.

3. Non-surgical treatments

Randomised controlled trials published in the 1990s established that 5-FU-based chemotherapy reduces the crude risk of colon cancer recurrence and mortality by as much as 10%.¹⁴ These publications led to a progressive change in practices. In France, it took only 4 years in patients under 65, and 6 years in those aged 65–74, to reach almost optimum values.¹⁵ Although there was some improvement over time, few patients over the age of 75 received adjuvant chemotherapy for stage III colon cancer (24%, 1997–1998 period).¹⁵ Data from Europe and Australia suggested that in the year 2000, only 20–25% of elderly patients received adjuvant chemotherapy,^{15–20} in comparison to 40–50% in the US^{21–29} (Table 2). More frequent use of adjuvant chemotherapy in elderly patients would reduce death from colorectal cancer. Data from the SEER programme suggested that, in patients older than 65

Table 1 – Aggregate data on treatment and stage at diagnosis for colorectal cancer according to age in 28 studies (see 4)

	65–74 years	75–84 years	≥85 years
Resection for cure	75%	73%	67%
No operation	6%	11%	21%
Emergency surgery	15%	18%	29%
TNM stage 1	15%	14%	10%
TNM stage 4	21%	22%	25%

Table 2 – Proportions of elderly stage III colon cancer patients treated with adjuvant chemotherapy; population-based data^a

	Author	Period of diagnosis	Age group				Comorbidity score		
			All cases (75+ y)	75–79 y	80–84 y	85+ y	0	1	2+
Australia	Morris et al.	1994–2001	17% [64%]	–	–	–	–	–	–
France	Phelip et al.	1995	18%	–	–	–	–	–	–
	Faivre-Finn et al.	1997–1998	24%	52%	10%	3%	–	–	–
Germany	Fietkau et al.	1999–2000	29%	–	–	–	–	–	–
The Netherlands	Lemmens et al.	1995–2001	–	20%	–	–	28%	16%	15%
USA	Potosky et al.	1995	35%	47%	–	24%	–	–	–
	Schrag et al.	1996	38%	58%	34%	8%	–	–	–
	Dobie et al.	1992–1996	–	56%[74%] ^b	30%[68%] ^c	8%[65%] ^d	59%[79%]	48%[77%]	47%[74%]
	Sundararayan et al.	1992–1996	52%	58%	32%	15%	59%	57%	33%
	Ayanian et al.	1996–1997	39%	–	48%	11%	{ 53% ^e 19% ^f	{ 47% ^e 9% ^f	{ 37% ^e 2% ^f
	Gross et al.	1993–1999	–	63% ^b	38% ^c	11% ^d	69%	55% ^g	39% ^h
	Neugut et al.	1995–1999	–	54%[63%]	21%[51%] ⁱ	–	56%[68%]	44%[61%]	39%[57%]
Switzerland	Cronin et al.	2000	52%	–	–	–	–	–	–
	Jessup et al.	2001–2002	–	69% ^j	–	39%	–	–	–
	Bouchardy et al.	1990–1996	13% ^k	–	–	–	–	–	–

a In square brackets: rate of adjuvant chemotherapy completion.

b Age group 76–80 y.

c Age group 81–85 y.

d Age group 86+ y.

e Age group 75–84 y.

f Age group 85+ y.

g 1–2 comorbid conditions.

h 3+ comorbid conditions.

i Age group 80+ y.

j Age group 70–79 y.

k Age group 70+ y.

years of age, treatment with 5-FU in node positive colon cancer was associated with a 34% reduction in mortality, a difference similar to that described in randomised studies.³⁰ Elderly patients have been under-represented in clinical trials, so it can be difficult to determine whether the benefits shown among trial participants pertain to older patients. However, a review of seven randomised trials indicated that the benefits of 5-FU-based chemotherapy in elderly people diminished only slightly with increasing age, and there was only a small increase in toxicity (in particular mucite).^{31,32} So, greater toxicity is an insufficient explanation for the decline in usage observed with advancing age. Elderly patients themselves may choose not to receive chemotherapy. However, when studied, older patients were just as likely as younger patients to accept chemotherapy, although after choosing to receive treatment they were less likely to accept major toxicity in exchange for added survival.³³ Furthermore, they have indicated that the primary determinant of their decision regarding chemotherapy was their physician's advice.³⁴ The physician's attitude may explain the low utilisation of adjuvant chemotherapy, in particular in Europe.

Some elderly patients may be unsuitable for chemotherapy due to pre-existing comorbidity. In a US study among patients 75 to 84 years of age, 53% received chemotherapy in the

absence of co-morbidity, 47% if there was one-comorbid condition and 37% if there were two²⁵ (Table 2). The corresponding percentages for patients aged 85 and older were 19%, 9% and 2%. In the Netherlands, 28% of patients aged 75 to 79 years old without comorbidity received adjuvant chemotherapy, compared to 15% of patients in this age group with comorbidity.¹⁶ However, despite the fact that chronic conditions appear to be a strong barrier to the receipt of adjuvant chemotherapy, there is a paucity of studies that were able to link specific comorbid conditions to outcome for colorectal cancer. A recent cohort study did not find any link between adjuvant chemotherapy and heart-failure, diabetes, and chronic pulmonary obstructive disease, regarding all-cause, condition-specific, or toxicity-related hospitalisation.²⁸

In view of the generally relatively low toxicity of chemotherapy in colon cancer and the increase in life expectancy, it can be concluded that a larger proportion of elderly patients, who are healthy enough to be operated on, could benefit from this treatment. The treatment decision for an individual patient should be based on the known benefit as opposed to the side effects and the impact on quality of life. In this context, discussion of the medical file within multidisciplinary consultancy meetings, including a geriatrician, is important. A recent survey in France indicated that

multidisciplinary consultancy meetings have yet to be fully developed, particularly for the elderly.³⁵ The importance that patients place on the physician's opinion makes it imperative for clinicians to fully inform their patients of the potential benefit of chemotherapy.

Local recurrence, following curative resection for rectal cancer, remains a substantial problem. A population-based study has reported a 5-year local recurrence rate of 25% (1976–2000 period).³⁶ These results demonstrate the importance of effective adjuvant treatment in addition to surgery. Adjuvant radiotherapy for rectal cancer has been shown to reduce local recurrence, and preoperative radiotherapy was found to be more effective than postoperative radiotherapy. The effectiveness of preoperative radiotherapy has also been demonstrated after optimal surgery including total mesorectal excision.³⁷

Current guidelines for patients with rectal cancer include adjuvant or neoadjuvant radiotherapy. Some data are available on the practice of radiotherapy in the elderly at a population level. They indicate that elderly patients are being undertreated compared to younger patients: 35% versus 79% in Burgundy over the 1994–1996 period.³⁸ There were some variations between countries: treatment among elderly patients stood at 36%–40% among SEER registries in the US (1992–1996 period),^{25,27,39} 35% in France (1994–1996),³⁸ 36% in Germany (1999–2000),²⁰ and 20%–50% in the Netherlands (1980–2000, 2000–2004)(40–42, Lemmens, submitted for publication) (Table 3). In the US, adjuvant treatment consisted of postoperative radiotherapy administered concurrently with chemotherapy. In France and in the Netherlands, preoperative radiotherapy has become the standard treatment regimen. Although radiotherapy is not always indicated in elderly patients because of severe comorbidity, it has not reached full implementation in this age group. The need for transportation between the home and the few radiotherapy centres can limit its use for elderly patients, although this aspect seems to be less important for patients receiving short-course preoperative radiotherapy (5 × 5 Gray). It has also been shown that elderly patients who underwent surgery plus pre or post operative radiotherapy develop more complications

than patients undergoing surgery alone (especially pneumonia and cardiac complications). It is possible that after use of total mesorectal surgery, the added value of radiotherapy among the elderly is limited.⁴¹ In order to optimise the risk benefit ratio for elderly patients, a comprehensive geriatric assessment is of critical importance.⁵⁰

4. Survival

In a review of the literature, postoperative mortality, i.e. mortality within 30 days of surgery, was three times higher in patients aged 75–84 and over six times more common in those aged 85 and over, compared with patients under 65 years of age.⁵ The increase in postoperative mortality with advancing age may be partly explained by comorbidity. An increasing frequency of respiratory, cardiovascular and thromboembolic complications has been reported in relation to age.⁹ However, a steady reduction in operative mortality has been reported over time,^{43,44} even though it is still higher than in younger patients. This is all the more noticeable as the proportion of patients who were offered surgery has increased. This has been achieved by improvement in the perioperative management of elderly patients, through evaluation and preoperative correction of associated medical conditions and by improvement of postoperative resuscitation.

The 5-year mean relative survival rate for elderly patients, reported in the EURO CARE-3 study, covering the period 1990–1994,⁴⁵ was 43%, higher for colon cancer (46%) than for rectal cancer (39%). The rate was similar in males (43%) and in females (44%). It was lower in younger patients since the 5-year relative survival rate was 57% in patients under 45, and 51% in patients aged 65 to 74. A slight improvement in survival in elderly patients was reported in the EURO CARE study. For colon cancer, the 5-year relative survival rates were 40% (1983–1985 period) and 48% (1992–1994 period). The corresponding rates for rectal cancer were 35% and 40%. The gap that has separated younger from elderly patients is decreasing. In France, among patients over 80, 5-year relative survival rates for colon cancer increased from 27.0% (1978–1981) to 47.8% (1995–1997), and for rectal cancer from 18.1% to 41.7%.⁵ Also in

Table 3 – Proportions of elderly stage I–III rectal cancer patients treated with pre- or postoperative radiotherapy (population-based data)

	Author	Period of diagnosis	Age group			
			All cases (75+ y)	75–79 y	80–84 y	85+ y
France	Faivre-Finn et al.	1994–1996	35%	35%	36%	34%
Germany	Fietkau et al.	1999–2000	36%	–	–	–
The Netherlands	Martijn et al.	1980–2000	20%	–	–	–
	Shahir et al.	1995–2001	36% ^a	–	–	–
	Vulto et al.	1995–2002	–	55% ^{b,c}	23%	–
	Lemmens et al.	2000–2004	–	58% ^d	42%	–
	Neugut et al.	1992–1996	37%	48%	35%	17%
USA	Ayanian et al.	1996–1997	40%	47%	14%	–
	Cronin et al.	2000	36%	–	–	–

a Age group 70+ y.

b Age group 65–79 y.

c Declining from 65% in absence of comorbidity, to 45% in presence of two or more comorbid conditions.

d Age group 70–79 y.

Table 4 – 5-year relative survival rates for colon and rectum cancers in Europe (EUROCARE – 3 data)

	COLON		RECTUM	
	all ages	≥75	all ages	≥75
France	59	52	58	45
Switzerland	56	53	57	54
Netherlands	54	51	55	53
Sweden	53	53	55	48
Finland	54	51	51	43
Italy	53	45	49	36
Portugal	47	45	43	44
England	46	44	46	42
Denmark	46	43	44	35
Slovakia	43	41	31	19
Slovenia	40	31	36	28
Estonia	40	31	32	23
Poland	30	21	29	21

the Netherlands a clear improvement in relative survival could be noted among these patients: from 39% (1975–1984) to 45% (2000–2004) for colon cancer, and from 29% to 49% for rectal cancer (Lemmens, personal communication). The improvement in survival can be attributed to the decrease in operative mortality and to the increase in proportion of patients resected for cure, which is associated with earlier diagnosis. The excess mortality rate is mainly observed during the first months after diagnosis.^{46,47} The older persons who survive the first year have a prognosis similar to younger ones. Late diagnosis, and comorbidities or physiological impairment can explain an early prognostic disadvantage. These impose limits on the use of potentially curative treatment. Comorbidity was shown to be an independent prognostic factor.⁹ Previous malignancy, cardiovascular diseases, chronic obstructive pulmonary disease, hypertension and diabetes decreased 5-year survival. Comorbidity also led to less frequent use of adjuvant therapy, thus contributing to its impact on survival rates. In contrast, older patients who are in good health, and who can undergo the same therapies as younger patients, have the same chances of survival.

There were also large variations in survival between countries among elderly patients (Table 4). Survival rates were dramatically lower in Eastern European countries compared to Western European countries.⁴⁶ Stage at diagnosis remained the major determinant of prognosis. In Burgundy, the 5-year relative survival rate in elderly patients was 85% for stage I, 65% for stage II, 35% for stage III and 4% for stage IV (1991–2000 period). This is probably the major determinant of survival differences between countries. In a study involving three European cancer registries, differences in rectal cancer survival were no longer significant after adjusting for stage.⁴⁸ It has also been shown that survival is related to the level of health investment.⁴⁹ Effective diagnosis and conditions of treatment depend on macroeconomic determinants, including total national expenditure on health.

5. Conclusion

There is growing interest in the management of CRC in the elderly. Although improvements have been achieved, in partic-

ular an improvement in resection rate and a decrease in operative mortality, there is evidence that there is still room for improvement in the use of adjuvant treatments. Comorbidities, which are particularly frequent in the elderly, increase the complexity of cancer management and affect survival. The comprehensive geriatric assessments, and multidisciplinary consultations, need to be put in place to select those who can benefit from standard treatment.

Conflict of interest statement

None declared.

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