

# Review papers

---

*Acta chir belg*, 2006, **106**, 149-157

## Survival of Rectal Cancer Patients in Belgium 1997-98 and the Potential Benefit of a National Project

*F. Penninckx, L. Van Eycken, G. Michiels, R. Mertens, C. Bertrand, D. De Coninck, K. Haustermans, A. Jouret, A. Kartheuser, N. Tinton, on behalf of the PROCARE working group\**

\* The PROCARE working group consists of delegates from all Belgian scientific organisations involved in the treatment of rectum cancer, i.e. the Belgian Section of Colorectal Surgery, a section of the Royal Belgian Society of Surgery (De Coninck D., Duinslaeger M., Kartheuser A., Penninckx F., Van de Stadt J., Vaneerdeweg W.), the Belgian Society of Surgical Oncology (Claeys D.), the Belgian Group for Endoscopic Surgery (Burnon D.), the Belgian Society of Radiotherapy – Oncology (Haustermans K., Scalliet P., Spaas Ph.), the Belgian Society of Pathology and the Digestive Pathology Club (Ectors N., Jouret A.), the Belgian Society of Medical Oncology (Bleiberg H., Humblet Y., Van Cutsem E.), the Belgian Group for Digestive Oncology (Laurent S., Van Cutsem E., Van Laethem J. L.), the Royal Belgian Society of Radiology (Op de Beeck B., Danse E.), the Société Royale Belge de Gastro-entérologie (Melange M., Rahier J.), the Vlaamse Vereniging voor Gastro-enterologie (Cabooter M., Pattyn P., Peeters M.), the Belgian Society of Gastro-intestinal Endoscopy (Buset M.). Are also represented : the Belgian Professional Surgical Association (Haeck L., Mansvelt B.), the Private Foundation Belgian Cancer Registry (Van Eycken E.). Penninckx F. chairs the PROCARE Workgroup.

**Key words.** Rectum cancer ; survival ; audit.

**Abstract.** *Background :* PROCARE, a Belgian multidisciplinary project on rectal cancer (RC), will be launched in 2006. Guidelines have been developed, but remain to be implemented.

*Aim :* A population-based study on RC treatment and outcome in Belgium and comparison with recent international benchmarks in order to better define targets that should be reached.

*Patients and methods :* Anonymous data of 3079 patients with rectal cancer registered in the National Cancer Registry in 1997 and 1998 were analysed. Observed (OS) and relative survival (RS) were compared with figures from nationwide projects and multi-centre studies.

*Results :* The 5-yr OS and RS were 46.6% and 58.5%, respectively. For patients with stage I-III tumours 5-yr OS was 57.1% and 5-yr RS 70.1%. Adjuvant or neo-adjuvant treatment was given in 54.8% stage II-III patients who were < 70 years old. There were marked differences between the provinces in the use of radiotherapy for stage II-III patients and in 5-yr RS for all stages. In stage IV, the median OS was 13 months and the 2-yr OS was 28%. Comparison with recent multi-centre trials indicates significant potential benefits from the PROCARE project : an absolute increase of the 5-yr OS by 10 to 20% after chemoradiotherapy and TME in stage II-III patients 75 years old or less, a 7-month increase of the median OS and an absolute 15% increase of the 2-yr OS in unresectable stage IV patients with combined chemotherapy.

*Conclusion :* Significant improvement seems to be achievable. Implementation of the PROCARE guidelines with quality assurance through prospective registration in a specific database, however, is a crucial prerequisite for credible audit of performance and feedback to individual teams.

### Introduction

Quantitative and qualitative improvement of outcome after rectal cancer treatment has been documented. Replacement of conventional rectal cancer surgery (blunt pelvic dissection) by sharp total mesorectal excision (TME) with preservation of the autonomic nerve plexuses (1) and the construction of a colo-anal anastomosis (2) with a reservoir or coloplasty (3-5), has led to quantitative and qualitative improvements in outcome. Pre-operative radiotherapy or combined chemoradiation (6-8) have further reduced the local recurrence rate (LRR) in

resectable, mobile rectum cancers, with an impact on APR rate (abdominoperineal resection with definitive colostomy). Thus, high quality surgery with pathologic assessment (9, 10) plays a key-role in the management of rectum cancer, but both its quality and its result also depend on pre-operative radiologic information (11, 12) and neo-adjuvant therapy in clinical stage II and III tumours, in particular when located in the middle or lower third of the rectum (7). Finally, major breakthroughs in the treatment of metastatic colorectal cancer have been reported in recent years using new drugs, combined chemotherapy and/or biologicals (13-17).

Multidisciplinary guidelines based on these achievements aim to improve the quality of care through standardisation, i.e. reduction of variability in routine practice. Variation in outcome between hospitals/teams treating rectum cancer patients has been reported (18-21). The relationship between case-load and outcome is much debated, but outcome can improve through implementation of recent knowledge in high- as well as in low-volume hospitals (20, 21).

Population-based audits reflect the overall quality of care in a region or nation. Multi-centre trials with specific protocols (guidelines) give an estimate of the optimally reachable quality of care. Implementation of guidelines on a regional or nationwide basis is challenging, but feasible (22-27). This type of quality assurance requires surveillance in a specific rectal cancer database and a profession-driven audit with feedback (28).

The aim of this population-based audit on rectal cancer treatment in Belgium was to assess overall performance and outcome variability, in an era when formal national multidisciplinary guidelines did not exist and specific workshops had not been organised. Recently, the Belgian scientific societies involved in rectal cancer treatment have reached consent concerning multidisciplinary guidelines (29). In 2006 a nationwide project on cancer of the rectum (PROCARE) will be launched. By comparing the Belgian results with those reported in large multi-centre prospective trials, performed in the same observation period, we aim to estimate the potential benefit of the PROCARE project.

## Patients and methods

All 3079 patients notified to the National Cancer Registry (NCR) with a diagnosis of rectal carcinoma between January 1997 and December 1998 were included in this study. Identification was based on code C-20 of the International Classification of Diseases (ICD-10) for rectum cancer below 16 cm from the anal verge.

The Belgian NCR is a non-compulsory population-based registry initiated in 1983. The general registration form includes information on: the unique patient code, postal code of residence, date of birth, sex, date of incidence, histological diagnosis, clinical and pathological tumour TNM stage, type and sequence of treatment modalities. This dataset does not include documentation on comorbidity, identity of the surgeon, type of operation, incidence of recurrent disease (local and/or distant). Hence, APR rate, disease free or cancer specific survival could not be calculated. The quality of about 55% of patient/tumour data is improved by linkage and summarization of individual records coming from physicians, pathologists, 2 provincial cancer registries (Antwerp, Limburg), and all sickness funds (health insurers). The identity of the patient is encrypted by the

data source itself. Analysis is made on anonymous data. All deaths registered by the sickness funds between 1/1997 and 12/2003 were linked to the NCR database for calculation of the observed survival. The cause of death is unknown.

Stage grouping was according to the 4<sup>th</sup> edition of the TNM classification (30) based on a combination of pathological staging (pTNM) and clinical staging (cTNM). pTNM was available in 1248 patients with stage I-III cancer. Presence of distant metastasis, as mentioned in the clinical staging, was accepted as stage IV (263 patients). Otherwise, staging was recorded as unknown for further analysis in this study.

Rectum cancer in Belgium is treated in about 113 hospitals. In view of the low number of patients per hospital entered in the 2-year observation period, inter-hospital variability of performance could not be assessed. Instead, variation per province was analysed.

## Analysis

Age was categorised into 5 groups: < 50, 50-59, 60-69, 70-79, 80 or more years. Patients were followed-up until death or for a minimum of 5 years. The Kaplan-Meier method was used to calculate the observed survival (OS) from the date of diagnosis. Relative survival (RS), a measure for disease-specific survival, was calculated as the ratio of the OS of the patients and the expected survival of an age and sex matched sample of the general Belgian population. The expected survival was based on data from the Belgian population life tables (31).

In order to assess the performance of rectal cancer treatment in Belgium, the results of this survey were compared with those reported in other population-based observational studies/audits. The potential benefit of the PROCARE project in resectable rectal cancer (stages I-III) was estimated by comparing Belgian results with those of recent large multi-centre trials on TME with or without radio(chemo)therapy. Also, the outcome in patients with metastatic rectum cancer was compared with recently published studies. Where appropriate and possible, our patients were matched to those reported, taking into account the most important prognostic factors related to survival, i.e. tumour stage and age. Survival rates were compared using the log rank test.

Statistical analysis was performed using SAS<sup>®</sup> software version SAS 9.1.3.

## Results

### Demographics

The mean age of the 3079 patients registered in the NCR database was 69.5 years (median 71 years; range 18-99). About 19% (587/3079) of the patients were 80 years old or more. Fifty-eight percent were male.

Table I

Age-standardised incidence rate of rectal cancer per province (European standard population)

Province	Incidence	Number of patients
1	14,7	621
2	7,3	185
3	14,9	393
4	6,5	51
5	11,9	371
6	14,2	515
7	7,6	256
8	7,9	218
9	20,3	348
10	8,9	53
11	6,7	68

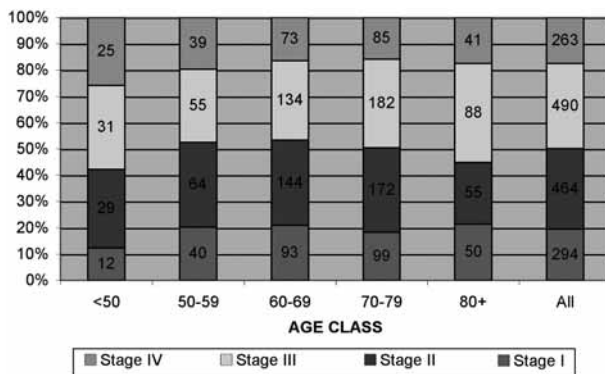


Fig. 1

Distribution of tumour stages per age class (values in the columns represent number of patients).

The incidence of rectal cancer seems to vary widely between provinces, although a rather comparable incidence was expected. This illustrates the non-compulsory nature of cancer registration for Belgium in 1997-1998 and the fact that in some provinces cancer registration is better organised or gets a better response than in others (Table I).

Tumour stage was known in 1511 patients (49.1%); it was based on pathology reports in 1248 patients with stage I-III cancer and on cTNM in 263 patients with stage IV cancer. Stage distribution was comparable in both sexes. More advanced stages were observed in the group < 50 years and in the group > 80 years with about 55% of patients presenting node positive or metastatic disease (Fig. 1).

#### Use of (neo)adjuvant treatment for Stage II and III rectum cancer

At the time of the observation period, the NIH Consensus Conference guideline of postoperative combined chemoradiation therapy for patients with stage II and III rectal cancer was well known (32). Although the

benefit of pre-operative, neo-adjuvant treatment for these types of tumour was not established at that time (the Swedish Rectal Cancer Trial was published in 1997), it was considered a valuable alternative.

The analysis of the therapeutic approach in stage II and III rectal cancer focused in particular on patients < 70 years old, as these are less likely to have contraindications for (chemo)radiation. Data on the therapeutic approach were available in 82% of patients with a known tumour stage. Neo-adjuvant or adjuvant radio(chemo)therapy was administered in 57.1% stage II (109/191) and in 52.6% stage III tumours (102/194), i.e. a total of only 54.8% of stages II-III patients < 70 years of age who had surgery (Table II). The application rate of radiotherapy for stage II-III tumours varied from 0% (0/6) to 67% (73/109) per province. The fact that 16% of patients with stage I tumours had radio(chemo)therapy may be related to down-staging after neo-adjuvant treatment or to adjuvant therapy after incomplete resection or intra-operative tumour break (R1 resection). Radio(chemo)therapy has been administered in 28% of patients with stage IV rectum cancer, which may be because of pre-operative under-staging or in the context of maximal treatment of the primary tumour with limited and/or resectable metastasis.

#### National survival results

The overall 5-year observed survival was 46.6%. It was age and stage dependent (Table III), but was not related to gender (data not shown). The 5-year relative survival rate was 58.5%. It was tumour stage dependent with an overall RS rate of less than 50% in stage III tumours and 10% in patients with metastatic disease (Table III). The cumulative 5-yr RS for all stages of rectal cancer varied between provinces from 48% to 71% (Fig. 2).

Table IV summarizes the comparison of this Belgian survey with the results of other national or regional audits for patients treated between 1987 and 1999. Although maximum effort was made to match the patient, tumour and treatment characteristics of the Belgian patients with those in the comparator groups, this could not always be achieved. TME was not implemented in the comparator surveys, except in Munich. The period of observation was much longer in Luxembourg and much earlier in the Netherlands and in Sweden than in Belgium. Outcome in Belgian patients was similar to that reported for Luxembourg (33), the Netherlands (22) and Sweden (6), but better than that observed in Denmark (34). OS and RS were slightly worse than in the Munich region (35).

#### Estimation of the potential benefits of the PROCARE project

TME may have been performed in some of the patients included in our survey, but no data are available for

Table II

Application of (neo)adjuvant radio(chemo)therapy according to age class and tumour stage in patients who had surgery  
Number of patients with percentage in parentheses

TNM stage	All ages			< 50 years			50-59 years			60-69 years			70-79 years			80+ years		
	N of pts	S only	S + RT	N of pts	S only	S + RT	N of pts	S only	S + RT	N of pts	S only	S + RT	N of pts	S only	S + RT	N of pts	S only	S + RT
I	257	216	41	11	10	1	36	27	9	81	61	20	87	78	9	42	40	2
II	379	212	167 (44)	25	6	19	54	26	28	112	50	62	146	91	55	42	39	3
III	431	255	176 (41)	29	13	16	43	20	23	122	59	63	169	93	76	76	68	8
II-III	810	467	343 (42)	54	19	35 (65)	97	46	51 (53)	234	109	125 (53)	315	184	131 (42)	118	107	11 (9)
IV	170	122	48	16	9	7	26	17	9	51	34	17	53	42	11	24	20	4

N number ; pts patients ; S surgery ; RT radiotherapy (either pre- or postoperative).

Table III

Observed (OS) and relative (RS) cumulative 5-year survival according to age class and tumour stage

TNM stage	All ages			0-49			50-59			60-69			70-79			80+		
	N of pts	OS	RS	N of pts	OS	RS	N of pts	OS	RS	N of pts	OS	RS	N of pts	OS	RS	N of pts	OS	RS
I	294	77.0	94.5	12	100	100	40	95.0	98.5	93	82.8	90.6	99	74.7	94.5	50	50.0	98.0
II	464	64.4	78.2	29	86.2	87.5	64	82.8	86.0	144	72.9	80.3	172	55.8	70.8	55	36.3	77.0
III	490	38.2	47.5	31	48.3	49.0	55	65.4	68.3	134	43.3	47.7	182	32.4	41.1	88	21.6	41.8
IV	263	8.3	10.2	25	28.0	28.4	39	17.9	18.7	73	2.7	3.0	85	5.8	7.3	41	2.4	5.2
unknown	1568	44.7	57.4	71	62.0	62.9	214	63.0	65.6	404	56.8	62.6	526	44.4	56.5	353	16.7	35.3
all stages	3079	46.6	58.5	168	61.3	62.2	412	65.3	67.9	848	55.6	61.2	1064	44.0	55.8	587	21.1	43.9

N number ; pts patients ; S surgery ; RT radiotherapy (either pre- or postoperative).

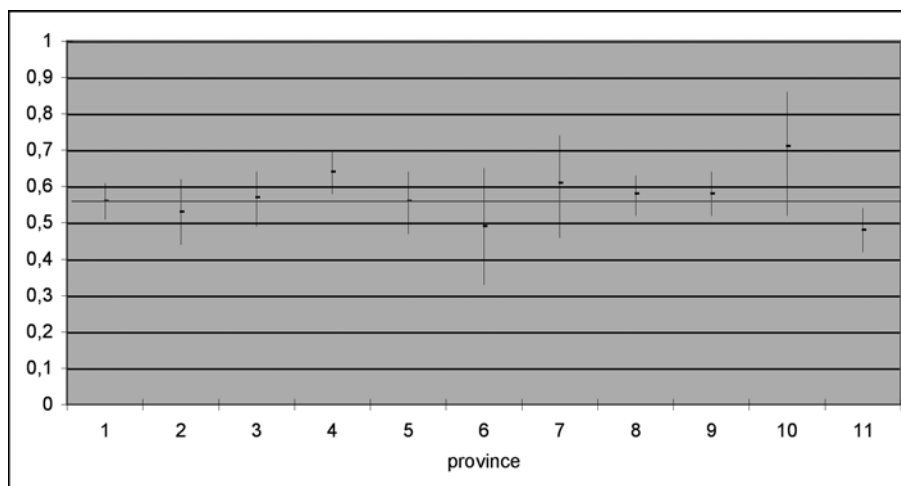


Fig. 2

5-year relative survival with 95% confidence intervals, standardised for age, per province (all stages included)

analysis. (Neo)adjuvant radio(chemo)therapy certainly was not performed in all those who would benefit from it (cf. supra). Neo-adjuvant radio(chemo)therapy is recommended in the PROCARE guidelines for patients with cStages II and III rectal cancer (29). Consequently, the potential benefit of the PROCARE project was estimated by comparison of the results of this Belgian sur-

vey with those reported in national audits or multi-centre trials in which TME with/without neo-adjuvant radiotherapy or radiochemotherapy was performed as a routine (Table V).

In the TME alone arm of the Dutch trial, the 5-yr OS was 63.5% (36). The Norwegian audit found a 61% 5-yr OS during a national TME project, postoperative

Table IV  
Comparison of performance with other national or regional audits

Reference	Region or country	Period of observation	Patients, tumour and treatment characteristics in comparator group	Outcome criterion	Comparator	Belgium 1997-1998
33	Luxembourg	1988-1999	St I-IV ; resection Rany St I ; resection Rany St II ; resection Rany St III ; resection Rany	5-yr OS	46% 81% 55% 34%	50% 77% 65% 39%
34	Denmark	1995-1996	all St ; no TME	5-yr RS	46.6%	58.5%
35	Munich	1996-98	all St ; 20.8% TME ; 9% neoadj. RT ; 40% adj. ther. all St ; 20.8% TME ; 9% neoadj. RT ; 40% adj. ther. St I ; patients with neo-adj. ther. excluded St II ; patients with neo-adj. ther. excluded St III ; patients with neo-adj. ther. excluded < 65 yr 65+ yr men women	5-yr OS 5-yr RS 5-yr RS 5-yr RS 5-yr RS 5-yr RS 5-yr RS 5-yr RS	52.7% 62.2% 96.9% 75.5% 58% 64.6% 61.0% 62.8% 61.5%	46.6% 58.5% 94% 76% 46% 64% 53% 57% 57%
22	Netherlands	1987-1990	St I-III ; no TME ; 38% adj. RT ; no neo-adj. RT	2-yr OS	77%	79.2%
6	Sweden	1987-1990	< 80 yrs ; St I-III ; no TME S only < 80 yrs ; St I ; no TME S only < 80 yrs ; St II ; no TME S only < 80 yrs ; St III ; no TME S only	5-yr OS 5-yr OS 5-yr OS 5-yr OS	48% 78% 64% 37%	64% 83% 64% 35%

St stage ; R type of resection ; TME total mesorectal excision ; neoadj. ther. neoadjuvant therapy ; adj. adjuvant ; RT radiotherapy ; S surgery  
OS observed survival ; RS relative survival.

Table V

Comparison of 5-year observed survival in Belgium 1997-1998 with results of national projects or multicentre randomised trials

Reference	Region or country	Period of observation	Patients, tumour and treatment characteristics in comparator group	Comparator	Belgium
27, 37	Norway	1993-1999	< 75 yrs ; pSt I-III ; TME ; 9% adjuvant RT	61%	64%
36	Netherlands	1996-1999	all ages ; cSt I-III (7% St IV incl.) ; TME	63.5%	57.1%
36	Netherlands	1996-1999	all ages ; cSt I-III (7% St IV incl.) ; 25 Gy RT + TME	64%	57.1%
25	Stockholm	1995-96	all ages ; cSt I-III ; TME or 25 Gy RT + TME ; R0 only ?	58.2%	57.1%
8	Germany	1995-2002	< 76 yrs ; cSt II-III (6% St IV incl.) ; 50.4 Gy RCT + TME	76%	
8	Germany	1995-2002	< 76 yrs ; cSt II-III (7% St IV incl.) ; TME + 50.4 Gy RCT	74%	
38	Germany	1995-2002	< 76 yrs ; cSt II-III (St IV and R1 excl.) ; 50.4 Gy RCT + TME	83%	58%
38	Germany	1995-2002	< 76 yrs ; cSt II-III (St IV and R1 excl.) ; TME + 50.4 Gy RCT	77%	58%
39	France	1993-2001	< 75 yrs ; cSt II-III up to 10 cm ; TME ? ; 45 Gy RT	66%	
39	France	1993-2001	< 75 yrs ; cSt II-III up to 10 cm ; TME ? ; 45 Gy RCT	66%	
40	EORTC	1993-2001	< 80 yrs ; cSt II-III ; TME recommended ; 45 Gy RT	64.8%	55%
40	EORTC	1993-2001	< 80 yrs ; cSt II-III ; TME recommended ; 45 Gy RCT	65.6%	55%

St stage ; TME total mesorectal excision ; RT radiotherapy ; RCT radiochemotherapy.

mortality (3%) included (27, 37). The effect of pre-operative 5 × 5 Gy radiation therapy followed by TME surgery has been documented in the Dutch trial with a 64.0% 5-yr OS (36). For comparison, the 5-yr OS in patients of any age with stage I-III rectal cancer was 57% in this Belgian survey. A 76% 5-yr OS was observed after neo-adjuvant 50.4 Gy radiochemotherapy followed by TME surgery in the German multi-centre trial randomising patients up to 75 years of age with

cStage II-III between pre- and postoperative radiochemotherapy (8). After exclusion of patients with stage IV disease and R1 resection, the 5-yr OS after neo-adjuvant radiochemotherapy and TME surgery was 83% (38). The abstracts from the French FFCO 9203 trial (39) and of the multinational EORTC 22921 trial (40) report a 5-year OS of 65-66% for cStage II-III tumours after neo-adjuvant radiotherapy with or without chemotherapy ; TME was recommended but the quality

of its performance is not yet reported. For comparison, the 5-yr OS in patients up to 75 years old with stage II-III cancer was 58% in this Belgian survey. These data indicate that the OS in patients with resectable rectal cancer could optimally be improved by more than an absolute 20%, i.e. a relative improvement of about 40%.

Finally, the outcome in stage IV patients can be improved. The median survival in patients with unresectable metastatic colorectal cancer has increased to more than 20 months since the introduction of combinations of irinotecan or oxaliplatin with continuous FA/5-FU (FOLFIRI or FOLFOX) (14). In second-line therapy, patients should receive oxaliplatin after irinotecan, or vice versa (13), resulting in a median OS of 20.2-21.5 months and a 2-yr survival of 41-45%. For comparison, in this Belgian survey, a median OS of 13 months and a 2-yr OS of 28% were observed in stage IV patients up to 75 years, indicating a potential for significant improvement.

## Discussion

Population-based audits of the treatment and outcome in patients with rectal cancer have been shown to contribute to the improvement of the quality of care (24-27). The retrospective analysis that we have performed can be criticised because of several shortcomings of the available database. The incompleteness of data is related to the non-compulsory and non-specific character of rectal cancer documentation. The fact that the database is not profession-driven could contribute to the lack of registration compliance by the physicians. The absence of precise data on the type of surgery does not permit evaluation of the APR rate nor of the incidence of temporary derivative stoma construction in cases of sphincter preservation. In this study, it has not been feasible to link the NCR data with information on the comorbidity or ASA-status of the patient, postoperative morbidity or in-hospital mortality. Histopathological evaluation of the quality of surgery is also missing (no data on the circumferential margin). LRR and disease-free survival can not be calculated, as non-lethal events occurring during follow-up are not registered. Cancer-specific survival can not be calculated if the cause of death during follow-up is unknown. It can, however, be substituted by relative survival calculations, as was done in this report. Finally, no feedback could be given in the current situation as the team or the hospital where the patient was treated was not included in the NCR data. Hence, prospective registration of all patients presenting rectal cancer in a specific, detailed database, with quality control of the data entered, is a *conditio sine qua non* for a credible audit with feedback to the individual health-providing teams in order to improve overall and individual performances. In Sweden, improved outcome after

rectum cancer treatment has been attributed to better surgery and a more selective use of radiotherapy, but most of all to an increased awareness of the treatment results and a focus on good, credible auditing (28). In spite of incomplete registration and the obviously very limited dataset in this audit, we feel that the results of this study permit some other important conclusions and indicate areas for significant potential improvement.

Many patients still present with advanced disease: 32.4% with node positive stage III and 17.4% with distant metastasis. We observed that node positive or metastatic rectum cancer was more frequent in patients < 50 and > 80 years old. This may indicate insufficient screening and poor public awareness of alarming symptoms in the younger age group, but it might also be partially related to sub-optimal management in the elderly.

The data available at the NCR mainly allowed survival to be assessed. The 5-year OS and RS were 46.6% and 58.5%, respectively. Survival was stage dependent, but comparable in both sexes. This outcome of patients treated in Belgium in 1997-1998 was not significantly different from that reported in national observational studies performed before the introduction of TME surgery in Sweden (6), the Netherlands (22) and Luxembourg (33). It should be noted that in these reports most patients were recruited in a period prior to this Belgian observation. Outcome in Belgian patients was better than that reported from Denmark (34), but slightly worse than in the Munich study (35). The latter may be related to the fact that TME resection was performed in 20.8% of their cases; moreover, (neo)adjuvant treatment was also more frequent in Munich (49%) than in Belgium (36%).

In Belgium, over 100 hospitals treat patients with rectal cancer. In the absence of guidelines and audit of their implementation, diagnostic and therapeutic variability is most likely. Because of the shortness of the observational period, therapeutic variability and differences in relative survival were assessed per province. This analysis indicates that (neo)adjuvant radiotherapy was only used in about 55% of stage II-III rectal cancer patients, supporting the suggestion from an earlier questionnaire based report (41) that a substantial number of these patients are under-treated. Relative survival also showed high variability between provinces, ranging from 48% to 71%. These data should be interpreted with caution because of the low number of registered patients in some provinces. It is evident that credible audit of inter-hospital variation and stimulating feedback can only be achieved by more complete registration, so that the results of individual teams/hospitals can be appropriately compared with national or international benchmarks after risk adjustments. This requires adequate tools as well as the effective collaboration of all professionals involved in the care of rectal cancer. The PROCARE

working group has produced multidisciplinary guidelines (29) and several of the scientific organisations, including local groups of specialists, have organised postgraduate courses, seminars and workshops in 2005. The Belgian Professional Surgical Association supports the project (42). A specific database has been set up at the National Cancer Registry for prospective registration on a voluntary basis, starting in 2006. The anonymous data will be audited by delegates from the PROCARE workgroup. Also, instruction/training has been organised by the respective scientific and professional organisations. The aim of the project is to improve outcome and reduce variability in quality of care. Several other national audits/projects have shown the feasibility of a major and complex undertaking like this (22, 24-27). Inter-hospital/team variation and differences in outcome is, of course, a delicate matter. The actual organisation of health care delivery and the willingness and dedication of teams and individual professionals to collaborate in a national project like PROCARE, are key factors. In contrast to other projects, PROCARE has preferred decentralised instruction/training and treatment of patients. Thus, no single team has been excluded from taking part in the PROCARE project. In Denmark, no hospital volume effects on 30-day mortality and 5-year survival were observed when data were adjusted for age, gender and tumour stage (20). These findings were explained by the fact that the excellent performance of some well trained surgeons working in medium- or lower-volume hospitals outweigh the overall influence of hospital type and volume. Major inter-hospital variation was observed in small as well as in medium and large sized Norwegian hospitals (21), and in non-academic as well as in academic German or Swedish hospitals (18, 43). Centralisation of RC treatment into large, specialised units therefore seems to be no guarantee of optimal care *per se*. These findings support the decentralised character of the PROCARE project. It is assumed that feedback on the performance of individual hospitals and teams will allow them to react whenever they would not perform according to the national standards or below the targets set up in national guidelines.

Survival is the single most important endpoint in the treatment of cancer patients. Comparison of the results of this Belgian audit with those of recent nationwide or multicentre prospective studies indicates a significant potential benefit of the PROCARE project. It might be argued that comparison with multi-centre trials is not completely correct because of biases in patient selection. Nonetheless, their results indicate the optimally reachable outcome. The 5-yr OS in patients of any age with stage I-III rectal cancer was 57% in this Belgian survey, and that of patients up to 75 years old with stage II-III rectal cancer was 58%. The recent trial of the German Rectal Cancer Study Group randomised patients with

stage II-III rectal cancer between pre- and postoperative chemo radiotherapy. TME resection was standard. They observed a 5-yr survival of 76 and 74%, respectively, with significantly reduced LRR, acute and long-term toxicity after neo-adjuvant treatment (8). Their survival rate increases to 83% in the neo-adjuvant arm and 77% in the postoperative arm, when patients with stage IV disease and R1 resection are excluded (38). The PROCARE multidisciplinary guidelines recommend neo-adjuvant treatment for comparable tumour stages. Consequently, the current 5-yr OS of 58% for stage II and III patients in Belgium could potentially increase to an optimum of about 80% in patients up to 75 years of age. Admittedly, the PROCARE project cannot reach this optimum outcome, because no patient will be excluded from registration. The implementation of TME with pathological quality control could improve, though to a more limited extent, the 5-yr OS of 86% in stage I rectal cancer in Belgium. Indeed, the 5-yr RS in these patients is currently 94%. The potential impact of routine and adequate TME on the LRR could not be assessed.

Another potential area for significant progress is patients with stage IV disease. Implementation of combined chemotherapy could result in almost doubling their median and 2-year survival.

## Conclusion

The outcome of rectal cancer treatment in Belgium in 1997-1998 was comparable with that reported in other countries before wide implementation of TME surgery and neo-adjuvant treatment. This retrospective study provides benchmark data to which the outcome of patients treated according to the multidisciplinary guidelines of the PROCARE project will have to be compared. Implementation of guidelines with quality assurance through registration in a specific database and feedback to individual teams has the potential for significant improvement, as indicated by the comparison of the results of this audit with those of recent prospective multi-centre studies on multimodality treatment of patients with resectable rectum cancer or combined chemotherapy for metastatic disease. The PROCARE project offers all Belgian professionals, involved in rectal cancer treatment, the opportunity to show their commitment to the improvement of the quality of health care delivered in rectal cancer patients.

## Acknowledgments

The PROCARE Workgroup thanks Mrs. Frie Hermans and Mrs. Martine Verstreken at the Foundation Belgian Cancer Registry for their dedicated support in collecting the data for this study.

The PROCARE workgroup also thanks the Foundation against Cancer, foundation of public interest (Stichting tegen

Kanker / Fondation contre le Cancer / Stiftung gegen Krebs) for financially supporting the specific rectal cancer database at the Belgian Cancer Registry.

The PROCARE project will be supported by the Ministry of Health (RIZIV/INAMI).

## References

- MACFARLANE J. K., RYALL R. D., HEALD R. J. Mesorectal excision for rectal cancer. *Lancet*, 1993, **341** : 457-460.
- PARKS A. G., PERCY J. P. Resection and sutured colo-anal anastomosis for rectal carcinoma. *Br J Surg*, 1982, **69** : 301-4.
- LAZORTHES F., FAGES P., CHIOTASSO P., LEMOZY J., BLOOM E. Resection of the rectum with construction of a colonic reservoir and colo-anal anastomosis for carcinoma of the rectum. *Br J Surg*, 1986, **73** : 136-8.
- PARC R., TIRET E., FRILEUX P., MOSZKOWSKI E., LOYGUE J. Resection and colo-anal anastomosis with colonic reservoir for rectal carcinoma. *Br J Surg*, 1986, **73** : 139-41.
- Z'GRAGGEN K., MAURER C. A., BUCHLER M. W. Transverse coloplasty pouch. A novel neorectal reservoir. *Dig Surg*, 1999, **16** : 363-6.
- SWEDISH RECTAL CANCER TRIAL. Improved survival with pre-operative radiotherapy in resectable rectal cancer. *N Engl J Med*, 1997, **336** : 980-7.
- KAPITEIJN E., MARIJNEN C. A. M., NAGTEGAAL I. D., PUTTER H., STEUP W.H., WIGGERS T., RUTTEN H. J. T., PAHLMAN L., GLIMELIUS B., VAN KRIEKEN J. H. J. M., LEER J. W. H., VAN DE VELDE C. J. H., THE DUTCH COLORECTAL CANCER GROUP. Pre-operative radiotherapy combined with total mesorectal excision for resectable rectal cancer. *New Engl J Med*, 2001, **345** : 638-646.
- SAUER R., BECKER H., HOHENBERGER W., RÖDEL C., WITTEKIND C., FIETKAU R., MARTUS P., TSCHMELITSCH J., HAGER E., HESS C. F., KARSTENS J. H., LIERSCH T., SCHMIDBERGER H., RAAB R., FOR THE GERMAN RECTAL CANCER STUDY GROUP. Pre-operative versus post-operative chemoradiotherapy for rectal cancer. *N Engl J Med*, 2004, **351** : 1731-40.
- QUIRKE P., DURDEY P., DIXON M. F., WILLIAMS N. S. Local recurrence of rectal adenocarcinoma due to inadequate surgical resection. Histopathological study of lateral tumour spread and surgical excision. *Lancet*, 1986, **2**, 996-9.
- NAGTEGAAL I. D., VAN DE VELDE C. J. H., VAN DER WORP E., KAPITEIJN E., QUIRKE P., VAN KRIEKEN H. J. M., AND THE PATHOLOGY REVIEW COMMITTEE FOR THE CO-OPERATIVE CLINICAL INVESTIGATORS OF THE DUTCH COLORECTAL CANCER GROUP. Macroscopic evaluation of rectal cancer resection specimen : clinical significance of the pathologist in quality control. *J Clin Oncol*, 2002, **20** : 1729-34.
- BEETS-TAN R. G., BEETS G. L., VLIEGEN R. F., KESSELS A. G., VAN BOVEN H., DE BRUINE A., VON MEYENFELDT M. F., BAETEN C. G., VAN ENGELSHOVEN J. M. Accuracy of magnetic resonance imaging in the prediction of a tumour-free resection margin in rectal cancer surgery. *Lancet*, 2001, **357** : 497-504.
- BROWN G., RADCLIFFE A. G., NEWCOMBE R. G., DALLIMORE N. S., BOURNE M. W., WILLIAMS G. T. Pre-operative assessment of prognostic factors in rectal cancer using high-resolution magnetic resonance imaging. *Br J Surg*, 2003, **90** : 355-64.
- TOURNIGAND C., ANDRÉ T., ACHILLE E., LLEDO G., FLESH M., MERY-MIGNARD D., QUINAUX E., COUPEAU C., BUYSSE M., GANEM G., LANDI B., COLIN P., LOUVET C., DE GRAMONT A. FOLFIRI followed by FOLFOX6 or the reverse sequence in advanced colorectal cancer : a randomized GERCOR study. *J Clin Oncol*, 2004, **22** : 229-37.
- GOLDBERG R. M., SARGENT D. J., MORTON R. F., FUCHS C. S., RAMANATHAN R. K., WILLIAMSON S. K., FINDLAY B. P., PITOT H. C., ALBERTS S. R. A randomized controlled trial of fluorouracil plus leucovorin, irinotecan, and oxaliplatin combinations in patients with previously untreated metastatic colorectal cancer. *J Clin Oncol*, 2004, **22** : 23-30.
- ANDRÉ T., BONI C., MOUNEDJI-BOUDIAF L., NAVARRO M., TABERNERO J., HICKISH T., TOPHAM C., ZANINELLI M., CLINGAN P., BRIDGEWATER J., TABAH-FISCH I., DE GRAMONT A., FOR THE MULTI-CENTRE INTERNATIONAL STUDY OF OXALIPLATIN/5-FLUOROURACIL/LEUCOVORIN IN THE ADJUVANT TREATMENT OF COLON CANCER (MOSAIC) INVESTIGATORS. Oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment for colon cancer. *N Engl J Med*, 2004, **350** : 2343-51.
- HURWITZ H., FEHRENBACHER L., NOVOTNY W., CARTWRIGHT T., HAINSWORTH J., HEIM W., BERLIN J., BARON A., GRIFFING S., HOLMGREN E., FERRARA N., FYFE G., ROGERS B., ROSS R., KABBINAVAR F. Bevacizumab plus irinotecan, fluorouracil, and leucovorin for metastatic colorectal cancer. *N Engl J Med*, 2004, **350** : 2335-42.
- VAN CUTSEM E. J., OLIVEIRA J., KATAJA V. V., ESMO GUIDELINES TASK FORCE. ESMO minimum clinical recommendations for the diagnosis, treatment and follow-up of advanced colorectal cancer. *Ann Oncol*, 2005, **16 Suppl 1** : i18-9.
- HERMANEK P. The impact of the surgeon's technique on outcome after treatment of rectal carcinoma. *Dis Colon Rectum*, 1999, **42** : 559-62.
- MARTLING A., CEDERMARK B., JOHANSSON H., RUTQVIST L. E., HOLM T. The surgeon as a prognostic factor after the introduction of total mesorectal excision in the treatment of rectal cancer. *Br J Surg*, 2002, **89** : 1008-13.
- HARLING H., BÜLOW S., MOLLER L. N., JORGENSEN T., THE DANISH COLORECTAL CANCER GROUP. Hospital volume and outcome of rectal cancer surgery in Denmark, 1994-99. *Colorectal Disease*, 2005, **7** : 90-95.
- WIBE A., ERIKSEN M. T., SYSE A., TRETLI S., MYRVOLD H. E., SOREIDE O., NORWEGIAN RECTAL CANCER GROUP. The effect of hospital caseload on long-term outcome after standardization of rectal cancer surgery at a national level. *Br J Surg*, 2005, **92** : 217-24.
- KAPITEIJN E., PUTTER H., VAN DE VELDE C. J. H., AND CO-OPERATIVE INVESTIGATORS OF THE DUTCH COLORECTAL CANCER GROUP. The impact of the introduction and training of total mesorectal excision on recurrence and survival in rectal cancer in the Netherlands. *Br J Surg*, 2002, **89** : 1142-49.
- ENGEL A. F., OOMEN J. L. T., EIJSBOUTS Q. A. J., CUESTA M. A., VAN DE VELDE C. J. H. Nationwide decline in annual numbers of abdomino-perineal resections : the effect of a successful national trial ? *Colorectal Disease*, 2003, **5** : 180-4.
- MARTLING A. L., HOLM T., RUTQVIST L. E., MORAN B. J., HEALD R. J., CEDERMARK B., FOR THE STOCKHOLM COLORECTAL CANCER STUDY GROUP AND THE BASINGSTOKE BOWEL CANCER RESEARCH PROJECT. The effect of a surgical training programme on outcome of rectal cancer in the county of Stockholm. *Lancet*, 2000, **356** : 93-6.
- MARTLING A., HOLM T., RUTQVIST L. E., JOHANSSON H., MORAN B., HEALD R. J., CEDERMARK B. The impact of a surgical training programme on rectal cancer outcomes in Stockholm. *Br J Surg*, 2005, **92** : 225-9.
- WIBE A., MOLLER B., NORSTEIN J., CARLSEN E., WIIG J. N., HEALD R. J., LANGMARK F., MYRVOLD H. E., SOREIDE O., FOR THE NORWEGIAN RECTAL CANCER GROUP. A national strategic change in treatment policy for rectal cancer – implementation of total mesorectal excision as routine treatment in Norway. A national audit. *Dis Colon Rectum*, 2002, **45** : 857-866.
- WIBE A., ERIKSEN M. T., SYSE A., MYRVOLD H. E., SOREIDE O., ON BEHALF OF THE NORWEGIAN RECTAL CANCER GROUP. Total mesorectal excision for rectal cancer – what can be achieved by a national audit ? *Colorectal Disease*, 2003, **5** : 471-477.
- PAHLMAN L., KARLBOM U. Teaching efforts to spread TME surgery in Sweden. *Recent Results Cancer Res*, 2005, **165** : 82-85.
- PROCARE multidisciplinary guidelines for the treatment of rectal cancer. [www.belsurg.org/imgupload/BSCRS\\_/PROCARE%20GUIDELINES%20printversie82005.pdf](http://www.belsurg.org/imgupload/BSCRS_/PROCARE%20GUIDELINES%20printversie82005.pdf).
- HERMANEK P., SOBIN L. H. eds. TNM classification of malignant tumours. Fourth edition, 2<sup>nd</sup> revision, Berlin Springer-Verlag : 1992.
- Belgium, Life tables 1997-1998, "Federal Public Service Economy, SMEs, Self-employed and Energy, Directorate-general Statistics Belgium, Service Demography".
- NIH CONSENSUS CONFERENCE. Adjuvant therapy for patients with colon and rectal cancer. *JAMA*, 1990, **264** : 1444-50.



33. SCHEIDEN R., SAND J., WEBER J., TURK P., WAGENER Y., CAPESIUS C. Rectal cancer in Luxembourg : a national population-based data report, 1988-1998. *BMC Cancer*, 2003, **3** : 27-35.
34. IVERSEN L. H., PEDERSEN L., RIIS A., FRIIS S., LAURBERG S., SORENSEN H. T. A population-based study of short- and long-term survival from colorectal cancer in Denmark 1977-1999. *Br J Surg*, 2005, **92** : 873-880.
35. KERR J., ENGEL J., ECKEL R., HÖLZEL D. Survival for rectal cancer patients and international comparisons. *Ann Oncol*, 2005, **16** : 664-672.
36. VAN DE VELDE C. ON BEHALF OF THE DUTCH COLORECTAL CANCER GROUP. Personal communication.
37. WIBE A. ON BEHALF OF THE NORWEGIAN RECTAL CANCER GROUP. Personal communication.
38. SAUER R. ON BEHALF OF THE GERMAN RECTAL CANCER STUDY GROUP. Personal communication.
39. GERARD J. P., BONNETAIN F., CONROY T., CHAPET O., BOUCHE O., CLOSON-DEJARDIN M. T., UNTEREINER M., LEDUC B., FRANCOIS E., BEDENNE L. Pre-operative radiotherapy  $\pm$  5 FU/folinic acid in T3-4 rectal cancers : results of the FFCD 9203 randomized trial. *J Clin Oncol*, 2005, **16S** : 3504.
40. BOSSET J. F., CALAIS G., MINEUR L., MAINGON P., RADOSEVIC-JELIC L., DABAN A., BARDET E., BENY A., OLLIER J. C., COLLETTE L. Pre-operative radiation in rectal cancer : the effect and timing of additional chemotherapy, 5-year results of the EORTC 22921 trial. *J Clin Oncol*, 2005, **16S** : 3505.
41. BEAUDUIN M., DENEUFBOURG J. M., DE NEVE W., HERMANS J., HOORNAERT M. T., SCALLIET P., SPAAS P., VANDERICK J., VAN DIJCKE M., VAN HOUTTE P., VYNCKIER S., WELTENS C. The management of rectal cancer in Belgium : a survey of our practice. *Acta Gastro-enterol Belg*, 2004, **67** : 9-13.
42. HAECK L. Het PROCARE project. De Geneesheer-Specialist, November, 2004, p. 6.
43. HOLM T., JOHANSSON H., CEDERMARK B., EKELUND G., RUTQVIST L. E. Influence of hospital- and surgeon-related factors on outcome after treatment of rectal cancer with or without pre-operative radiotherapy. *Br J Surg*, 1997, **84** : 657-63.

F. Penninckx  
 Department of Abdominal Surgery  
 UZ Gasthuisberg  
 Herestraat 49  
 3000 Leuven, Belgium  
 Tel. : 32-16-344265  
 Fax : 32-16-344832  
 E-mail : freddy.penninckx @uz.kuleuven.ac.be