Chapter 8

Risk factors for excess mortality in the first year after curative surgery for colorectal cancer

GA Gooiker*
JWT Dekker*
E Bastiaannet
LGM van der Geest
JWS Merkus
CJH van de Velde
MWJM Wouters
RAEM Tollenaar
GJ Liefers

On behalf of the steering committee of the 'Quality Information System Colorectal
* Both authors contributed equally to this article

Annals of Surgical Oncology, 2012 mar 7 (Epub ahead of print)
Abstract

Aims: Thirty-day mortality after surgery for colorectal cancer may vastly underestimate 1-year mortality. This study aims to quantify the excess mortality in the first postoperative year of stage I-III colorectal cancer patients and to identify risk factors for excess mortality.

Methods: All 2131 patients who were operated with curative intent for stage I-III colorectal cancer in the Western region of the Netherlands, between January 1 2006 and December 31 2008, were analyzed. Thirty-day mortality and relative survival were calculated. Also Relative Excess Risks of death (RER) were estimated using a multivariable model.

Results: Thirty-day mortality was 4.9%. One-year mortality was 12.4%. Risk factors for Excess Mortality (EM) in the first postoperative year for colon cancer patients were emergency surgery (EM 29.7%, RER (Relative Excess Risk) 2.5 (95%CI 2.5-5.0)), a Charlson score >1 (EM 12.6%, RER 2.3 (1.5-3.7)), stage II or III disease (EM 14.9%, RER 3.9 (1.9-8.1)) and postoperative adverse events (EM 22.6%, RER 2.1 (1.4-3.2)).

Conclusions: The 30-day mortality rate highly underestimates the risk of dying in the first year after surgery, with excess 1-year mortality rates varying from 15 to 30%. This excess mortality was especially prominent in patients with co-morbidities, higher stages of disease, emergency surgery, and postoperative surgical complications.
Introduction

Adverse postoperative events are most often recorded as 30-day mortality and postoperative complications. Large studies show that colorectal cancer surgery can be considered as high risk with reported postoperative mortality and complication rates around 5% and 20-40% respectively. 1-4

For the prognosis of colorectal cancer patients that undergo curative surgery, adverse postoperative events constitute a determining factor. Several studies showed that complications are of prognostic importance, because they can cause delayed mortality. 5-6 Furthermore, specific complications such as anastomotic leaks are associated with local recurrences and reduced survival.7-9 Elderly patients with severe co-morbidities, lower social economic status, a stage III tumor or preoperative tumor complications, have been shown to be at higher risk for postoperative adverse events.10-12

Earlier studies have shown that 30-day mortality after surgery for colorectal cancer vastly underestimates 1-year mortality,13-14 even in young colorectal cancer patients that were operated with curative intent. Furthermore, Dekker et al showed that 1-year excess mortality (1-year mortality adjusted for expected mortality in the general population) was the main determining factor for age related survival differences: after surviving the first year, elderly had the same cancer related survival as younger patients.14 This suggests that there may be a prolonged impact of the assault of surgery. Up to date little information exists on the etiology of the excess mortality in the first postoperative year. Because of the lack of reported determinants of excess mortality in the contemporary literature, we set out to determine the role of co-morbidity, emergency surgery and postoperative complications, expecting that these factors are main determinants for 1-year excess mortality. Especially in elderly patients where the incidence of co-morbidity is higher and emergency surgery and postoperative complications occur more frequently.
The identification of risk factors would help to stratify patients according to their risk. Moreover, risk factors may be modifiable and targeted optimization of care may result in an improved prognosis.

Therefore, the first aim of this study was to quantify the excess mortality in the first postoperative year of stage I-III colorectal cancer patients operated with curative intent according to several patient and tumor characteristics. The second aim of this study is to identify risk factors for excess mortality in the first postoperative year.

**Methods**

**Data**

In the Netherlands, all newly diagnosed malignancies are registered in the nationwide population based Netherlands Cancer Registry (NCR). The Leiden Cancer Registry, part of the NCR, collects data on all cancer patients diagnosed in one of the nine affiliated hospitals in the Midwestern part of the Netherlands. This region comprises one university hospital, six teaching hospitals and two non-teaching hospitals and serves a population of 1.7 million inhabitants.

Independently trained data managers collect data from the original patient files after receiving an automatic report from the Dutch pathology reporting system “PALGA.” Information on patient characteristics, tumor characteristics, treatment, hospital of diagnosis and/or treatment and follow-up are recorded. Tumor site and morphology are coded according to the International Classification of Diseases for Oncology (ICD-0). Cancers are staged according to the TNM classification of Malignant Tumors, 6th edition. The quality of the data is high, and completeness is estimated to be at least 95%.

In 2006, a regional audit for colorectal cancer surgery (KIC) was started in the nine
affiliated hospitals of the Leiden Cancer Registry. The data collection was extended to data that reflected quality of care and case mix factors. These prospectively collected data were used for benchmarking and feedback on each hospitals process, ultimately to improve the quality of care in the entire region. Data were collected on patient demographics (age, sex, co-morbidities and socio-economic status (SES)), tumor characteristics (localization, TNM staging) and treatment characteristics ((neo-) adjuvant treatment, type of surgery, emergency, hospital of treatment, surgical complications and length of stay). Apart from ASA scores, completeness of data was more than 98%.

**Patients**

All patients who had a resection of stage I, II or III tumor of the colon (C18), the recto-sigmoid (C19) or the rectum (C20) from 1 January 2006 to 31 December 2008 in one of the affiliated hospitals, were identified (patients with a stage IV tumor, with a tumor of the appendix and patients who did not undergo a resection of the tumor, were excluded). Age was categorized in younger than 65 years, 65 to 74 years and 75 years and older. Co-morbidity was recorded according to a slightly modified version of the Charlson index, used by the Dutch Cancer Registry. ASA scores were categorized as ASA I and II or ASA III and IV. Missing data from the ASA score were included as a separate category. SES was categorized as low, intermediate and high, based on area-based data concerning income, employment and education, provided by the Netherlands Institute for Social Research.[19] Surgical complications comprised superficial wound infections, abdominal wall problems (i.e., dehiscence), deep infections, and intra-abdominal complications including bleeding, ileus, abscess or anastomotic leaks. As a substitute for overall complications (both surgical and non-surgical such as pulmonary or cardiac events), a prolonged length of stay was used, which was defined as a hospital admission of 15 days or longer after surgery. Vital status of all patients was obtained actively on a regular basis through linkage of the cancer registry data with the integrated database of the municipal registry and the central bureau for genealogy. Follow-up was completed until January 1 2010.
**Statistical analysis**

All analyses were done for colon and rectum cancer patients separately. Stratified by several characteristics, 30-day mortality, 1-year overall mortality (all causes) and 1-year excess mortality rates were calculated. Excess mortality was calculated by 

\[
\frac{(\text{Observed number of deaths in the 1st year} - \text{Expected number of deaths in the matched general population})}{\text{Number of patients}}.
\]

Expected number of deaths was calculated using national life tables matched on age, sex and year of incidence. Survival curves of the relative survival in the first year were constructed. Relative survival is the preferred way to describe the prognosis of elderly cancer patients as it takes into account the risk of dying of other causes than the disease of interest in the absence of cause of death in the database. Relative survival was calculated as the ratio of the observed survival among the cancer patients and the expected survival. Relative Excess Risks of death (RER) with p-value were estimated using a multivariable generalized linear model with a Poisson distribution, based on collapsed relative survival data, using exact survival times.

**Results**

From January 1, 2006 until December 31, 2008, 2131 patients had a colorectal resection in one of the nine affiliated hospitals of the CCCW, for stage I-III colorectal cancer; 1407 for colon cancer and 724 for rectal cancer. Table 1 shows characteristics of the study population for colon and rectal cancer patients. Colon patients were older, more often female, had more comorbidity and more often required emergency surgery.

**30-day mortality, 1-year mortality and excess mortality**

The overall observed 30-day mortality was 4.9%, the 1-year mortality 12.4%. Median follow-up time was 24.6 (range 0.03-47.9) months. All patients had follow up for at least one year unless they died previously. Table 2 shows crude overall mortality and excess mortality rates of stage I-III colon and rectal cancer patients in the first year after surgery, according to several characteristics. The observed 1-year
Table 1
Characteristics of the population according to localization

| Variables          | Colon cancer | Rectal cancer |
|--------------------|--------------|---------------|
| **Age (years)**    |              |               |
| <65                | 371          | 264           |
| 65-74              | 390          | 236           |
| ≥75                | 646          | 244           |
| **Sex**            |              |               |
| Male               | 672          | 406           |
| Female             | 735          | 318           |
| **Stage**          |              |               |
| I                  | 234          | 214           |
| II                 | 661          | 231           |
| III                | 512          | 279           |
| **Emergency**      |              |               |
| Emergent           | 188          | 17            |
| Elective           | 1219         | 707           |
| **ASA**            |              |               |
| I / II             | 633          | 450           |
| III / IV / V       | 297          | 21.1          |
| Unknown            | 477          | 33.9          |
| **Charlson**       |              |               |
| 0                  | 757          | 444           |
| 1                  | 358          | 160           |
| 2 or more          | 292          | 120           |
| **Complications**  |              |               |
| No                 | 1155         | 559           |
| Yes                | 252          | 165           |
| **Hospital stay**  |              |               |
| < 15 days          | 956          | 471           |
| ≥ 15 days          | 419          | 238           |
| Unknown            | 32           | 15            |
| **SES**            |              |               |
| High               | 449          | 243           |
| Intermediate       | 480          | 241           |
| Low                | 478          | 240           |
| **Total**          | **1407**     | **724**       |
Table 2
Overall 30-day and 1-year mortality, and 1-year excess mortality.

|                  | Colon 30-day mortality | Colon 1-year overall mortality | Colon 1-year excess mortality | Rectal 30-day mortality | Rectal 1-year overall mortality | Rectal 1-year excess mortality |
|------------------|------------------------|--------------------------------|-------------------------------|-------------------------|---------------------------------|-------------------------------|
| Overall          | 6.3                    | 14.8                           | 10.9                          | 2.4                     | 7.9                             | 4.8                           |
| **Sex**          |                        |                                |                               |                         |                                 |                               |
| Male             | 7.7                    | 16.2                           | 12.1                          | **3.5**                 | 9.6                             | 6.2                           |
| Female           | 4.9                    | 13.5                           | 9.8                           | **0.9**                 | 5.7                             | 3.2                           |
| **Age**          |                        |                                |                               |                         |                                 |                               |
| <65              | **1.6**                | 5.9                            | 5.3                           | **0.4**                 | 2.3                             | 1.6                           |
| 65-74            | 4.1                    | 12.3                           | 10.2                          | **0.4**                 | **6.8**                         | 4.5                           |
| ≥75              | **10.2**               | 21.4                           | 14.6                          | **6.7**                 | **15.6**                        | **8.9**                       |
| **SES**          |                        |                                |                               |                         |                                 |                               |
| High             | **4.7**                | 12.9                           | 9.0                           | 2.5                     | 7.0                             | 3.5                           |
| Intermediate     | **8.5**                | 15.2                           | 11.5                          | 2.9                     | 9.1                             | 6.7                           |
| Low              | **5.4**                | 16.1                           | 12.1                          | 1.7                     | 7.5                             | 4.2                           |
| **ASA**          |                        |                                |                               |                         |                                 |                               |
| I/II             | **1.9**                | 7.9                            | 4.4                           | **1.0**                 | **5.1**                         | **2.3**                       |
| III/IV           | **11.1**               | 24.9                           | 19.9                          | **6.5**                 | **14.6**                        | **10.2**                      |
| Unknown          | **9.0**                | 17.6                           | 13.8                          | **2.6**                 | **9.5**                         | **6.6**                       |
| **Stage**        |                        |                                |                               |                         |                                 |                               |
| I                | 6.8                    | 9.8                            | 6.1                           | 1.9                     | 4.7                             | 1.3                           |
| II               | 5.9                    | 13.8                           | 9.5                           | 3.0                     | 8.2                             | 5.4                           |
| III              | 6.5                    | **18.4**                       | **14.9**                      | 2.2                     | 10.0                            | 7.1                           |
| **Emergency**    |                        |                                |                               |                         |                                 |                               |
| Emergent         | **18.1**               | 32.9                           | 29.7                          | N.A.                    |                                 |                               |
| Elective         | **4.4**                | **11.9**                       | **8.0**                       |                         |                                 |                               |
| **Comorbidity**  |                        |                                |                               |                         |                                 |                               |
| No               | 4.3                    | 10.5                           | 7.7                           | 0.3                     | 4.4                             | 1.7                           |
| Yes              | **7.7**                | **17.8**                       | **13.2**                      | **4.5**                 | **11.5**                        | **8.0**                       |
| **Charlson**     |                        |                                |                               |                         |                                 |                               |
| 0                | **4.1**                | **10.8**                       | **7.5**                       | **0.7**                 | **4.7**                         | **1.8**                       |
| 1                | 6.7                    | 17.0                           | 12.6                          | 3.8                     | 10.0                            | 6.9                           |
| 2 or more        | **11.3**               | 22.3                           | 17.5                          | **6.7**                 | **16.7**                        | **13.0**                      |
| **Complications**|                        |                                |                               |                         |                                 |                               |
| No               | **5.2**                | **12.4**                       | **8.3**                       | **1.4**                 | **6.1**                         | **2.9**                       |
| Yes              | **11.1**               | **25.8**                       | **22.6**                      | **5.5**                 | **13.9**                        | **11.2**                      |
| **Hospital stay**|                        |                                |                               |                         |                                 |                               |
| < 15 days        | 5.4                    | 9.8                            | 6.2                           | 2.3                     | 5.5                             | 3.0                           |
| ≥ 15 days        | 8.4                    | 26.5                           | 22.0                          | 2.5                     | 11.3                            | 7.2                           |
| Unknown          | 3.1                    | 9.4                            | 5.0                           | 0.0                     | **26.7**                        | **24.3**                      |

Bold and italic: p-value<0.05 for the different value within a variable.
mortality rates of patients older than 75, were 21% and 16% for colon and rectal patients respectively. High excess mortality rates were observed in colon cancer patients with ASA III/IV (19.9%), a stage III tumor (14.9%), a Charlson score of 2 or higher (17.5%) and in patients with postoperative surgical complications (22.6%) or a prolonged length of stay (22%). Of all colon cancer patients with an emergency resection, 33% died in the first year, an excess mortality of 30%. In rectal cancer patients high excess mortality rates were observed in elderly (8.9%), patients with a Charlson 2 or higher (13%) and patients with postoperative complications (11.2%).

**Figure 1** shows relative survival curves of all patients in the cohort (a) and an example of relative survival in a specific subgroup: colon cancer patients treated in an emergency setting (b).

**Figure 1**
Relative Survival in the first year: all patients (a) and colon patients treated in emergency setting (b).
The red line marks the 30th day after surgery. The blue line represents the relative survival in the first year. The space between the red dotted line and the blue line represents the excess mortality after 30 days and within the first year after surgery.
Risk factors for excess mortality in the first year

Figure 2 shows all identified risk factors for 1-year mortality for colon and rectal cancer patients separately. The effect is represented as adjusted relative excess risk (RER) for 1-year mortality. In table 3 (supplementary) the results of univariate and multivariable analysis for risk factors for excess mortality in the first year are shown.

For colon cancer patients, significant risk factors for excess mortality in the first year after surgery, were a stage III tumor (RER 2.6 (1.3-5.3), p <0.001), a Charlson score > 1 (RER 2.5 (1.6-4.0) p = 0.001), an emergency resection (RER 3.3 (2.5-5.0), p < 0.001) and postoperative surgical complications (RER 2.1 (1.4-3.3) p < 0.001). Particular co-morbidities, that increase the risk of excess mortality, were a previous tumor (RER 1.8 (1.2-2.8) p = 0.009), pulmonary disease (RER 2.1 (1.3-3.2) p =0.001), gastro-intestinal disease (RER 2.0 (1.1-3.6) p=0.02) and neurological disease (RER 1.7 (1.0-2.8) p= 0.04).

For rectal cancer patients risk factors for excess mortality in the first year, were age ≥ 75years (RER 7.0 (1.8-27.4) p=0.009), Charlson score > 1 (RER 5.2 (1.7-15.9) p =0.01), and postoperative surgical complications (RER 5.9 (1.3-26.8). Particular co-morbidities that increase the risk were, hypertension (RER 2.4 (1.1-5.5) p=0.04), vascular disease (RER 3.4 (1.3-9.3) p=0.02), kidney disease (RER 7.9 (2.4-26.5) p=0.001) and neurological disease (RER 3.3 (1.0-10.4) p=0.04).

Figure 2
Factors associated with 1-year Relative Survival in multivariable analysis for colon and rectal cancer patients separately. At the Y-axis, the effect size is represented as adjusted relative excess risk (RER) for 1 year mortality, compared to the reference group, which always has a RER of 1.
| Event = DOD at 1 Year | Colon | Rectal |
|------------------------|-------|--------|
| | Univariate & Multivariable | Univariate & Multivariable |
| | RER (95%CI) | p-value | RER (95%CI) | p-value | RER (95%CI) | p-value |
| Age | | | |
| <65 | 1 | 0.0001 | 1 | 0.004 | 1 | 0.01 |
| 65-74 | 2.0 (1.1-3.6) | 1.8 (1.0-3.3) | 2.8 (0.7-11.0) | 1.6 (0.4-7.6) |
| ≥75 | 3.2 (1.9-5.4) | 2.6 (1.5-4.5) | 6.2 (1.7-22.0) | 7.0 (1.8-27.4) |
| Sex | | | |
| Male | 1 | 0.2 | 1 | 0.3 | 1 | 0.2 | 1 | 0.1 |
| Female | 0.8 (0.5-1.1) | 0.8 (0.6-1.2) | 0.5 (0.2-1.3) | 0.4 (0.1-1.3) |
| Charlson | | | |
| 0 | 1 | 0.0004 | 1 | 0.004 | 1 | 0.01 |
| 1 | 1.8 (1.1-2.8) | 2.0 (1.3-3.2) | 3.8 (1.0-14.1) | 3.1 (0.8-11.3) |
| 2 or more | 2.6 (1.7-4.0) | 2.5 (1.6-4.0) | 7.7 (2.3-26.3) | 5.2 (1.7-15.9) |
| Hospital | | | |
| cont | 1.1 (1.0-1.2) | 1.0 (1.0-1.1) | 1.0 (0.8-1.2) | 1.0 (0.8-1.2) |
| Stage | | | |
| I | 1 | 0.006 | 1 | 0.002 | 1 | 0.3 |
| II | 1.6 (0.8-3.2) | 1.3 (0.6-2.6) | 4.4 (0.4-48.8) | 5.7 (0.9-36.2) |
| III | 2.5 (1.3-5.1) | 2.6 (1.3-5.3) | 5.8 (0.5-62.4) | 3.9 (0.7-24.1) |
| Emergency | No | 1 | <0.001 | 1 | <0.001 | 1 | 0.001 | 1 | 0.02 |
| Yes | 5.0 (3.3-10.0) | 3.3 (2.5-5.0) |
| Resection | Right sided | 1 | 0.01 | 1 | 0.03 |
| Left sided | 1.4 (0.9-2.2) | 0.7 (0.4-1.2) |
| Sigmoid | 0.6 (0.4-1.0) | 0.5 (0.3-0.9) |
| Complications | No | 1 | <0.001 | 1 | <0.001 | 1 | 0.001 | 1 | 0.02 |
| Yes | 3.1 (2.1-4.4) | 2.1 (1.4-3.3) | 4.2 (1.8-9.9) | 5.9 (1.3-26.8) |
| Hospital stay | Short | 1 | <0.001 | 1 | 0.003 | 1 | 0.002 | 1 | 0.002 |
| Long | 4.0 (2.7-5.9) | 2.1 (1.4-3.2) | 2.5 (1.0-6.3) | 0.4 (0.1-2.1) |
| Unknown | 0.8 (0.1-6.6) | 0.7 (0.1-6.5) | 9.9 (2.7-35.9) | 8.6 (2.4-31.7) |
Discussion

The excess mortality in the first year after surgery for stage I-III colorectal cancer is high. Overall, 12.4 % of all patients died within the first year, compared to a 4.9 % 30- day mortality rate. Thus, the 30-day mortality rate highly underestimates the risk of dying in the first year after surgery. After adjustment for expected mortality in the general population, patients with co-morbidities, patients with stage III tumors, patients requiring emergency resection, and patients with postoperative surgical complications were at higher risk for excess mortality, with excess 1-year mortality rates varying from 15 to 30%.

The present study is the first detailed population based study, quantifying excess mortality after colorectal cancer surgery with curative intent, and examining risk factors for excess mortality within the first year. Clinical, accurate data of the Netherlands Cancer Registry were used, and variables not only comprised age and stage, but also data on co-morbidities, emergency and postoperative complications were available. Moreover relative survival and excess mortality rates were used as outcome measures. This also takes into account mortality which is not attributable to the examined disease or the treatment of the disease.

The results in this study should be interpreted with regard to several limitations inherent to its observational design. In the univariate and multivariable analysis potential confounders were examined and added to the model (shown in supplementary table). In calculations of expected mortality, patients with severe comorbidity may not match well with the general population. This could have led to a slight underestimation of the expected mortality in this group, resulting in a lower excess mortality.

Furthermore, only data on postoperative surgical complications were available. To estimate the impact of both surgical and non-surgical complications (for example pneumonia, delirium, cardiac event or urinary tract infection), a prolonged length
of stay was used as a substitute of postoperative complications in general. In this study, a prolonged length of stay was defined as a stay of 15 days or longer. An uneventful postoperative period is unlikely to result in a longer hospital stay, and therefore, it can function as a proxy for overall complications. This assumption is in line with a study of Cohen et al, who demonstrated a mean length of stay after colorectal surgery of 16 days in the presence of complications versus 6 days when no complications occurred. In the present study a prolonged length of stay occurred in 30.4% of the patients. This is also consistent with findings in literature.

Acknowledging these limitations, the present study provides valuable information, showing that 30-day mortality underreports postoperative mortality after colorectal surgery. This is consistent with previous studies. Visser et al reported a doubling of 30-day mortality to 9.1% at 90 days after surgery. A previous study from our group showed that 1-year excess mortality was the main determinant for age related survival differences. In the present data, the steepest decline in relative survival was observed during the first 7 to 11 months after surgery. The excess mortality was especially high in patients with comorbidities, stage III disease, emergency surgery and postoperative surgical complications or a prolonged length of stay. These risk factors have been described before as risk factors for postoperative mortality and survival. However, these reports did not adjust for expected mortality in the general population, thereby not taking into account the risk of dying of other causes than colorectal cancer.

The aim of identifying risk factors for 1-year excess mortality was to find targets for improvement of patient care. However, these risk factors may not be easily malleable.

**Comorbidity**

The prevalence of comorbid disease is increasing with the aging population and improvements in modern medicine. Patients with comorbidity may have less biological reserve and comorbidities alter organ functions. More research is needed on these mechanisms and the influence of comorbidities on postopera-
tive outcomes. Obviously, optimizing peri-operative care to reduce surgical risk by thorough preoperative assessment and by additional supportive measures may improve the prognosis of patients. A multidisciplinary approach with integrated chronic disease management in cancer patients also in the post-hospital period seems warranted.

**Stage III disease**
Patients with stage III disease had an increased risk of excess 1-year mortality. This could be due to cancer recurrences. Although it is unlikely a large part of early mortality is due to cancer recurrences in patients operated with curative intent. An earlier study on relapses in these patients showed that only a very limited number of patients had a recurrence within the first year. Furthermore, only ten percent of patients with a recurrence die within one year.27

**Emergency surgery**
Emergency surgery has consistently been demonstrated to be a major risk factor for adverse outcome in colorectal surgery. Efforts should be made to reduce the number of patients in need of an emergent intervention. In this respect national screening programs could be helpful. If colorectal cancer could be identified at an earlier (asymptomatic) stage, it could be expected the need for emergent surgery can be reduced.

**Postoperative surgical complications or a prolonged length of stay**
Also patients with postoperative surgical complications or a prolonged length of stay had an increased risk for excess mortality in the first year. These results compare to a recent study of Greenblatt et al.5 They showed that readmission after colectomy, due to a postoperative complication, was predictive for 1-year mortality. Two recent studies of Ghaferi et al showed that differences in death after major complications were the primary determinant of variation of mortality between hospitals.28-29 This indicates that effective management of postoperative complications may reduce postoperative mortality and improve patient outcomes. This
provides a potential target for improvement of the quality of cancer care. Not only prevention of complications, but also early recognition and aggressive treatment of complications can improve patient outcomes. Identifying structures, processes and best practices to reduce the occurrence of complications and improve the management of complications should have priority. Although randomized controlled trials are pivotal for determination of efficacious interventions, large cohort studies and comparative effectiveness research are essential to fill critical gaps in defining optimal strategies for complication management. 30

Conclusions
In conclusion the excess mortality in the first postoperative year after colorectal cancer surgery is high and reflects postoperative risk more accurate than 30-day mortality. The presence of co-morbidities, a stage III tumor, emergency resection, and postoperative surgical complications were predictive for excess mortality, with excess 1-year mortality rates as high as 15 to 30%. These risk factors may not be easily modifiable. Nevertheless, their identification is important to develop tailored management of high risk patients. Moreover, identifying effective strategies for both prevention and treatment of complications could have the potential to improve patient outcomes.

Acknowledgements
The authors would like to acknowledge the professional network of surgical oncologists, the steering group of the KIC-project and the Comprehensive Cancer Centre the Netherlands for their advice, and the registrars of the Leiden Cancer Registry for the collection of the data. The additional data collection in the KIC-project was financially supported by the ZOLEON foundation.
Reference List

(1) van Gijn W, Gooiker GA, Wouters MW, Post PN, Tollenaar RA, van de Velde CJ. Volume and outcome in colorectal cancer surgery. Eur J Surg Oncol. Sep 2010;36 Suppl 1:S55-63.

(2) Paun BC, Cassie S, MacLean AR, Dixon E, Buie WD. Postoperative complications following surgery for rectal cancer. Ann Surg. May 2010;251(5):807-818.

(3) Morris EJ, Taylor EF, Thomas JD, et al. Thirty-day postoperative mortality after colorectal cancer surgery in England. Gut. Jun 2011;60(6):806-813.

(4) Al-Refaie WB, Parsons HM, Habermann EB, et al. Operative outcomes beyond 30-day mortality: colorectal cancer surgery in oldest old. Ann Surg. May 2011;253(5):947-952.

(5) Greenblatt DY, Weber SM, O'Connor ES, LoConte NK, Liou JI, Smith MA. Readmission after colectomy for cancer predicts one-year mortality. Ann Surg. Apr 2010;251(4):659-669.

(6) Maniku K, Bacchetti P, Leung JM. Prognostic significance of postoperative in-hospital complications in elderly patients. I. Long-term survival. Anesth Analg. Feb 2003;96(2):583-589, table of contents.

(7) McArdrle CS, McMillan DC, Hole DJ. Impact of anastomotic leakage on long-term survival of patients undergoing curative resection for colorectal cancer. Br J Surg. Sep 2001;88(9):1150-1154.

(8) Law WL, Choi HK, Lee YM, Ho JW, Seto CL. Anastomotic leakage is associated with poor long-term outcome in patients after curative colorectal resection for malignancy. J Gastrointest Surg. Jan 2007;11(1):8-15.

(9) Mirnezami A, Mirnezami R, Chandrakumaran K, Sasapu K, Sagar P, Finan P. Increased local recurrence and reduced survival from colorectal cancer following anastomotic leak: systematic review and meta-analysis. Ann Surg. May 2011;253(5):890-899.

(10) Bentrem DJ, Cohen ME, Hynes DM, Ko CY, Billimoria KY. Identification of specific quality improvement opportunities for the elderly undergoing gastrointestinal surgery. Arch Surg. Nov 2009;144(11):1013-1020.

(11) Janssen-Heijnen ML, Maas HA, Houterman S, Lemmens VE, Rutten HJ, Coebergh JW. Comorbidity in older surgical cancer patients: influence on patient care and outcome. Eur J Cancer. Oct 2007;43(15):2179-2193.

(12) Ingraham AM, Cohen ME, Billimoria KY, et al. Comparison of hospital performance in nonemergency versus emergency colorectal operations at 142 hospitals. J Am Coll Surg. Feb 2010;210(2):155-165.

(13) Visser BC, Keegan H, Martin M, Wren SM. Death after colectomy: it’s later than we think. Arch Surg. Nov 2009;144(11):1021-1027.

(14) Dekker JW, van den Broek CB, Bastiaannet E, van de Geest LG, Tollenaar RA, Liefers GJ. Importance of the first postoperative year in the prognosis of elderly colorectal cancer patients. Ann Surg Oncol. Jun 2011;18(6):1533-1539.

(15) International Classification of Diseases for Oncology. Third edition. Geneva: WHO;2000.

(16) UICC. TNM Classification of Malignant Tumours. Sixth Edition. New York: Wiley-Liss; 2002.

(17) Schouten LJ, Hoppener P, van den Brandt PA, Knottnerus JA, Jager JJ. Completeness of cancer registration in Limburg. The Netherlands. Int J Epidemiol. Jun 1993;22(3):369-376.

(18) Schouten LJ, Jager JJ, van den Brandt PA. Quality of cancer registry data: a comparison of data provided by clinicians with those of registration personnel. Br J Cancer. Nov 1993;68(5):974-977.

(19) Bastiaannet E, de Craen AJ, Kuppen PJ, et al. Socioeconomic differences in survival among breast cancer patients in the Netherlands not explained by tumor size. Breast Cancer Res Treat. Jun 2011;127(3):721-727.

(20) Cohen ME, Billimoria KY, Ko CY, Richards K, Hall BL. Variability in length of stay after colorectal surgery: assessment of 182 hospitals in the national surgical quality improvement program. Ann Surg. Dec 2009;250(6):901-907.
(21) Alves A, Panis Y, Mathieu P, Mantion G, Kwiatkowski F, Slim K. Postoperative mortality and morbidity in French patients undergoing colorectal surgery: results of a prospective multicenter study. Arch Surg. Mar 2005;140(3):278-283, discussion 284.

(22) Read WL, Tierney RM, Page NC, et al. Differential prognostic impact of comorbidity. J Clin Oncol. Aug 1 2004;22(15):3099-3103.

(23) Robbins AS, Pavluck AL, Fedewa SA, Chen YF, Ward EM. Insurance status, comorbidity level, and survival among colorectal cancer patients age 18 to 64 years in the National Cancer Data Base from 2003 to 2005. J Clin Oncol. Aug 1 2009;27(22):3627-3633.

(24) Janssen-Heijnen ML, Houterman S, Lemmens VE, Louwman MW, Coebergh JW. Age and co-morbidity in cancer patients: a population-based approach. Cancer Treat Res. 2005;124:89-107.

(25) Yancik R. Cancer burden in the aged: an epidemiologic and demographic overview. Cancer. Oct 1 1997;80(7):1273-1283.

(26) Pal SK, Hurria A. Impact of age, sex, and comorbidity on cancer therapy and disease progression. J Clin Oncol. Sep 10 2010;28(26):4086-4093.

(27) Kobayashi H, Mochizuki H, Morita T, et al. Timing of relapse and outcome after curative resection for colorectal cancer: a Japanese multicenter study. Dig Surg. 2009;26(3):249-255.

(28) Ghaferi AA, Birkmeyer JD, Dimick JB. Complications, failure to rescue, and mortality with major inpatient surgery in medicare patients. Ann Surg. Dec 2009;250(6):1029-1034.

(29) Ghaferi AA, Birkmeyer JD, Dimick JB. Variation in hospital mortality associated with inpatient surgery. N Engl J Med. Oct 1 2009;361(14):1368-1375.

(30) Dreyer NA, Garner S. Registries for robust evidence. JAMA. Aug 19 2009;302(7):790-791.
