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Original article

Inter-hospital variation in resection rates of colon cancer in the Netherlands: A nationwide study

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ABSTRACT

Introduction: Hospital of diagnosis is shown to have an impact on the probability of undergoing a resection in different types of gastrointestinal cancer. The aim of this study was to investigate the inter-hospital variation in resection rates and its impact on survival among patients with non-metastatic colon cancer.

Methods: All patients diagnosed with non-metastatic colon cancer between 2009 and 2014 were selected from the Netherlands Cancer Registry. Multilevel logistic regression was used to examine the variation in resection rates among hospitals. The effect of variation in surgical resection on overall survival was assessed using Cox regression analyses. Relative survival was used as an estimate for disease-specific survival.

Results: 38164 patients, treated in 95 different hospitals, were included in the analysis. After adjustments, resection rates varied between hospitals from 88 to 99%. This variation increased among patients older than 75 years, from 79 to 98%. Crude overall 5-year survival was 64%. After adjustment, no significant difference in overall or relative survival between hospitals with higher and lower resection rates was observed.

Conclusion: Resection rates are important to consider when interpreting hospital outcomes. There is a significant variation in resection rates in patients with non-metastatic colon cancer among hospitals in the Netherlands. This variation increases in the elderly. No significant effect on survival was found. This could imply that undertreatment may play a role as well as that some patients might not benefit from surgery.

Introduction

Surgical outcome in colorectal cancer has significantly improved over the last years [1]. Simultaneously, resection rates seem to have decreased in the Netherlands. Resection rates for colon cancer (metastatic cancer included) have dropped from 89.9% in 1995–1998 to 81.3% in 2008–2012 [2]. Where non-operative management of rectal cancer is gaining prominence, surgery remains the only curative modality in colon cancer [3]. In an ageing population, frailty and its subsequent perioperative risk might play an important role in the decrease in resection rates [4]. Nonetheless, although postoperative morbidity and mortality increase with age, elderly patients benefit from surgery [5] and have the same cancer specific survival benefit as younger patients as long as they get through the postoperative phase [6].

Colon surgery is widely performed. Previous studies have shown that the probability of undergoing surgery is associated with hospital of diagnosis for several gastro-intestinal cancers [7–9].

In the last decade, more attention is being drawn to health care outcomes and hospital performances. In oncological care the importance of measuring quality has been acknowledged by the

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initiation of several clinical audits like the Dutch ColoRectal Audit (DCRA) [10]. The DCRA registers hospital outcomes of colorectal cancer surgery. Not only the outcome of surgery is relevant to assess, but rather the hospital performance for their entire colorectal cancer population. When considering hospital performance, differences in resection rates are important for interpreting outcome measurements.

While differences in resection rates between hospitals could be consequential to differences in casemix, they could also suggest a different approach in decision-making and preoperative work-up. Some physicians may be more conservative when treating frail and older patients. It is important to know how this affects survival in these patients.

The aim of this study was to investigate the variation in proportion of colon cancer patients undergoing surgery among hospitals in a nationwide cohort of patients in the Netherlands while adjusting for several patient and tumor factors. The association between surgical treatment probability and overall and relative survival was also assessed.

Methods

Data collection

Data were extracted from the Netherlands Cancer Registry (NCR). This registry covers the total Dutch population of 17 million inhabitants and contains data of all newly diagnosed cancer patients in the Netherlands. The main source of information is the national pathology archive (PALGA), which sends weekly notifications of all cancer cases. Once a year, the registry is linked with the national hospital discharge register. Completeness is estimated to be at least 95%. Data on patient and tumor characteristics, diagnosis and treatment and morphology are routinely extracted from the medical records by trained registration clerks of the NCR. Anatomical site of the tumor is registered according to the International Classification of Disease – Oncology (ICD-O) [11]. Tumors are staged as defined by the UICC TNM classification valid at time of diagnosis [12]. The vital status is obtained by annual linkage to the Municipal Personal Records Database, which registers all deceased patients in the Netherlands.

Information on cause of death is not available in this registry. The present study did not require approval from an ethics committee in the Netherlands.

Study population

Patients with non-metastatic colon cancer were eligible for this study. All patients with a cM0 colon cancer diagnosed between 2009 and 2014 were included. Patients were divided into age groups: <75 years and ≥75 years. Tumor localization was divided into anatomical subsites: proximal colon (coecum, ascending colon, hepatic flexure, transverse colon and splenic flexure; C18.0, C18.2–18.5), distal colon (descending colon and sigmoid; C18.6–18.7) and other/NOS (C18.8–18.9). For patients with double tumors with the same date of resection, the most extensive tumor was included. Patients with double tumors with different dates of resection and patients with neuro-endocrine tumors were excluded. Also patients who underwent polypectomy without subsequent resection were excluded.

Definitions

The resection rate of a hospital of diagnosis was defined as the proportion of patients diagnosed in that respective hospital who underwent resection, regardless of the hospital in which the resection was performed. Resection included surgical resections.

Survival time was defined as the time from diagnosis to death, last follow-up date or end of the study period at February 1st, 2016 for patients who were still alive.

Statistical analyses

Differences in crude resection rates by patient and tumor characteristics were analyzed using Chi-square tests.

Because patients from one hospital are not independent of each other, a multilevel logistic regression model was constructed to predict the likelihood of undergoing resection (yes/no). The model additionally included the variables age, gender, period of diagnosis, subsite, clinical T, clinical N, morphology and differentiation grade. In case of missing values on variables, these were taken into account as separate categories of the respective variables. Each patient's adjusted probability of resection was given by formula $P = e^L/(1 + e^L)$, where L is the calculated value from the logistic regression for that particular patient. Next, the mean adjusted probability of resection for each hospital of diagnosis was defined as the mean adjusted resection probability of the patients diagnosed in that hospital. The variation in resection probabilities between hospitals was tested using ANOVA with Bonferroni correction. Similar analyses were performed for the age groups <75 years and ≥75 years separately.

The hospitals were categorized into four groups according to the adjusted resection probabilities of the hospitals. Crude 1- and 5-year overall survival in each of the groups was calculated by means of Kaplan-Meier. The impact of the variation in resection probabilities among hospitals on overall survival was analyzed using multivariable Cox regression analyses, thereby adjusting for age, gender, period of diagnosis, subsite, tumor stage, morphology, differentiation grade and chemotherapy. Analyses were performed for the age groups <75 years and ≥75 years separately and repeated for patients conditional on surviving the first year after diagnosis. Additionally, crude 1- and 5-year relative survival was used as an estimate for disease-specific survival. It reflects survival of cancer patients after adjustment for survival of the general population with the same age and gender distributions. For the calculation of relative excess risks of dying for the different categories of adjusted resection probabilities, regression models with a Poisson error structure were fitted. Again age, gender, period of diagnosis, subsite, tumor stage, morphology, differentiation grade and chemotherapy were included in the models and analyses were performed for the age groups <75 years and ≥75 years separately.

P values below *0.05* were considered statistically significant. SAS/STAT® statistical software (SAS system 9.4, SAS Institute, Cary, NC) was used for all analyses.

Results

A total of 41495 patients were diagnosed with non-metastatic colon cancer between January 2009 and December 2014. Patients were excluded for several reasons: 65 (1%) patients had a neuro-endocrine tumor; 1482 (4%) patients had a double tumor; and 1784 (4%) patients underwent polypectomy without subsequent resection. Finally, 38164 patients were included in the study. The median age of the study population was 73 years. There were slightly more male than female patients (51 vs. 49%, Table 1). The overall surgical resection rate was 94% (35774 patients). Resection rates decreased with age: from 97% for patients aged <75 years to 89% for patients aged ≥75 years. A small increase in the use of surgery was seen over the study period (93% versus 95% for the periods 2009–2010 and 2013–2014, respectively). Patients were treated for colon cancer in 95 different hospitals, with the number

Table 1
Patient and tumor characteristics of patients with non-metastatic colon cancer.

	Number of patients N (%)	Resection rate (%)	*P*-value*
Age			
<75	21,644 (56.7)	97.4	<0.0001
≥75	16,520 (43.3)	88.9	
Gender			
Male	19,569 (51.3)	94.3	<0.0001
Female	18,595 (48.7)	93.1	
Period of diagnosis			
2009–2010	12,122 (31.8)	93.3	<0.0001
2011–2012	12,737 (33.4)	93.2	
2013–2014	13,305 (34.8)	94.6	
Subsite			
Proximal colon	21,044 (55.1)	93.7	<0.0001
Distal colon	16,165 (42.4)	94.3	
Colon NOS/other	955 (2.5)	85.5	
Clinical T			
1	847 (2.2)	94.3	<0.0001
2	1931 (5.1)	96.4	
3	6754 (17.7)	96.5	
4	4676 (12.2)	89.0	
X	23,956 (62.8)	93.7	
Clinical N			
0	23,015 (60.3)	96.5	<0.0001
1	6129 (16.1)	94.8	
2	1249 (3.3)	91.4	
X	7771 (20.3)	85.1	
Morphology			
Mucinous adenocarcinoma	4742 (12.4)	97.9	<0.0001
Signet-ring cell carcinoma	408 (1.1)	92.9	
Adenocarcinoma	33,014 (86.5)	93.2	
Differentiation grade			
Good/moderate	27,652 (72.5)	98.2	<0.0001
Poor/undifferentiated	5310 (13.9)	96.5	
Unknown	5202 (13.6)	67.4	

*P-value indicates significance of the Chi-square test.

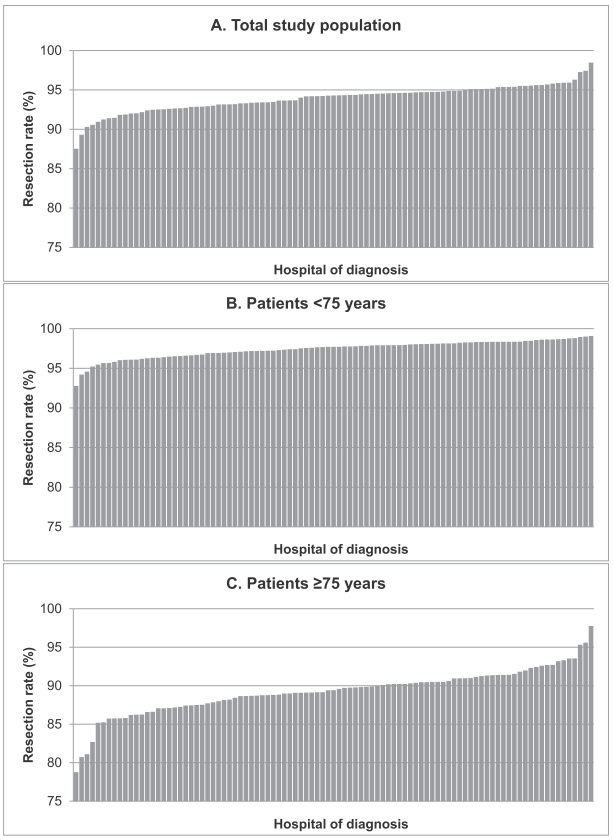

Fig. 1. Multilevel adjusted hospital variation in resection rates for patients with non-metastatic colon cancer, for the total study population (A, n = 38,164) and by age group (B, n = 21,644; C, n = 16,520)
Adjustments were made for age, gender, period of diagnosis, subsite, clinical T, clinical N, morphology and differentiation grade. Each bar represents one hospital.

of diagnoses ranging between 41 and 884. In total 9691 patients (25%) received postoperative chemotherapy.

After adjustment for several tumor and patient factors the surgical resection rate differed significantly between hospitals ($p < 0.0001$), ranging between 88% and 99% (Fig. 1). When comparing the age group younger than 75 years versus 75 years or older, the variation increased with age (93–99% in patients <75 versus 79–98% in patients ≥75 years). The number of diagnoses in the hospitals with the lowest and highest resection rate were respectively 16 and 131 for patients aged <75 years and 249 and 15 for patients aged ≥75 years. Patients aged <75 years underwent an extended resection (i.e. (sub)total colectomy) instead of a partial resection (i.e. hemicolectomy, transverse resection or sigmoid resection) slightly more often than patients aged ≥75 years (6.0% versus 4.4%, $p < 0.0001$). The proportion of patients undergoing an emergency resection was comparable for patients aged <75 years and patients aged ≥75 years (7.1% versus 7.3 respectively, $p = 0.452$).

Besides hospital of diagnosis, other factors associated with surgical resection rate were age, period of diagnosis, subsite of the tumor, clinical T, clinical N, morphology and differentiation grade.

Median follow-up time for the total study population was 46.8 months and crude overall 1 and 5 year survival were 87% and 64% respectively. The crude 1 and 5 year overall survival rates of patients according to the adjusted mean probability of resection in hospital of diagnosis are shown in Table 2. In univariable analysis, survival was lower in patients diagnosed in hospitals with a lower probability of undergoing resection in both age groups ($p < 0.0001$ for patients aged <75 years, $p = 0.0268$ for patients aged ≥75 years). However, after adjusting for patient, tumor and treatment characteristics in multivariable analysis, no significant difference in survival could be found, neither in the age group of patients <75 years, nor in the group with patients ≥75 years. All other variables included in the model (age, gender, period of diagnosis, subsite, stage, morphology, differentiation grade and chemotherapy) were associated with overall survival in both age groups (results not shown).

When univariable analyses were repeated only for patients who survived the first year after diagnosis, they were no longer significant ($p = 0.627$ for patients aged <75 years, $p = 0.711$ for patients aged ≥75 years). The crude 5 year overall survival rates and adjusted hazard ratios for death for these patients are presented in Table 3.

Table 4 presents the crude 1 and 5 year relative survival rates and relative excess risks of dying. No statistically significant differences were found.

Discussion

The present study shows a variation between hospitals in the proportion of patients who undergo surgical resection for non-metastatic colon cancer. This variation increases further in the elderly. After adjustment for casemix, no significant differences in crude 1 and 5 year overall and relative survival could be found between hospitals with higher and lower resection rates. Also when assessing the relative excess risk of dying, no differences were observed.

The inter-hospital variation in this study increased in the

Table 2
Crude 1- and 5-year overall survival and multivariable Cox proportional hazards analysis of overall survival for patients with non-metastatic colon cancer, by age group.

Age group	Probability of resection (%)[a]	Number of patients N	Crude 1-year overall survival (%)	Crude 5-year overall survival (%)	Adjusted hazard ratio[b] HR (95% CI)
<75 years	92–95	1356	91.8	73.6	1.11 (0.98–1.26)
	96	5615	92.3	75.3	1.05 (0.97–1.14)
	97	7514	94.1	77.1	1.01 (0.94–1.09)
	98–99	7159	94.6	77.7	1.00 (reference)
≥75 years	78–87	5085	77.9	46.8	0.98 (0.92–1.05)
	88–89	5919	79.1	47.8	1.01 (0.95–1.08)
	90	2558	78.6	48.8	1.04 (0.96–1.13)
	91–97	2958	81.4	49.5	1.00 (reference)

[a] Patients are grouped according to the adjusted mean probability of resection of the hospital where they were diagnosed.
[b] Adjusted for age, gender, period of diagnosis, subsite, tumor stage, morphology, differentiation grade and chemotherapy.

Table 3
Crude 5-year overall survival and multivariable Cox proportional hazards analysis of overall survival for patients with non-metastatic colon cancer, conditional on surviving the first year, by age group.

Age group	Probability of resection (%)[a]	Number of patients N	Crude 5-year overall survival (%)	Adjusted hazard ratio[b] HR (95% CI)
<75 years	92–95	1230	81.1	1.04 (0.89–1.23)
	96	5148	82.0	0.98 (0.89–1.09)
	97	7031	82.3	0.99 (0.91–1.09)
	98–99	6742	82.4	1.00 (reference)
≥75 years	78–87	3901	60.8	0.97 (0.88–1.06)
	88–89	4622	61.1	0.99 (0.91–1.09)
	90	1988	62.7	0.95 (0.85–1.07)
	91–97	2382	61.5	1.00 (reference)

[a] Patients are grouped according to the adjusted mean probability of resection of the hospital where they were diagnosed.
[b] Adjusted for age, gender, period of diagnosis, subsite, tumor stage, morphology, differentiation grade and chemotherapy.

Table 4
Crude 1- and 5-year relative survival and relative excess risks of dying for patients with non-metastatic colon cancer, by age group.

Age group	Probability of resection (%)[a]	Number of patients N	Crude 1-year relative survival (%)	Crude 5-year relative survival (%)	Relative excess risk[b] (95% CI)
<75 years	92–95	1356	92.4	79.4	1.12 (0.95–1.32)
	96	5615	93.2	80.7	1.07 (0.95–1.32)
	97	7514	95.0	82.6	0.99 (0.89–1.09)
	98–99	7159	95.5	83.2	1.00 (reference)
≥75 years	78–87	5085	83.2	71.4	0.94 (0.83–1.06)
	88–89	5919	84.8	73.1	1.01 (0.90–1.14)
	90	2558	84.1	74.7	1.06 (0.92–1.23)
	91–97	2958	87.2	75.4	1.00 (reference)

[a] Patients are grouped according to the adjusted mean probability of resection of the hospital where they were diagnosed.
[b] Adjusted for age, gender, period of diagnosis, subsite, tumor stage, morphology, differentiation grade and chemotherapy.

elderly, with some hospitals having resection rates of less than 80% in patients older than 75 years. This is in concordance with a previous study that also found lower resection rates in older patients [13]. For older patients, colorectal cancer surgery is associated with a higher risk of postoperative complications and as a result, decreased survival; in the present study significantly lower 1-year crude overall and relative survival are observed in older patients. Comorbidity and frailty are important factors contributing to a higher risk of postoperative complications [14–16]. A functional decline after surgery is observed as well [16]. It is therefore not surprising that elderly patients tend to be treated less aggressively than their younger counterparts. However, compared to other countries the resection rates among the older patients remain relatively high [17]. The rate of laparoscopic surgery in the Netherlands has increased over the last years. From 2010 to 2013 an increase of 37%–58% was observed [18]. Laparoscopic surgery is associated with a significant decrease in cardiopulmonary complications, especially in the elderly [18]. This may be one of the causes of the relatively high resection rates. Furthermore, there is an increasing number of hospitals in the Netherlands that has prehabilitation programs for elderly patients. These programs include physiotherapy, monitoring by a dietary consultant and also close involvement of a geriatrician. Although exact numbers are not available, this might have influenced the increasing number of older patients that underwent resection as well.

It remains unclear if there is an optimal resection rate; is it better to perform surgery on the majority of older patients with non-metastatic colon cancer or does a considerable group not benefit from surgery at all? There are several considerations that advocate surgery. As stated before, an increasing number of patients undergoes laparoscopic resection Patients more frequently maintain their preoperative functional status after laparoscopic surgery [19]. To optimize surgery in elderly patients, studies and clinical practice may have to focus more on the preoperative phase; prehabilitation i.e. optimizing the patient's condition could result in less postoperative morbidity and mortality [20]. Higher resection rates in the elderly might then be warranted and quality of life maintained. Although at present, solid evidence for the usefulness of prehabilitation is still lacking for these patients [21].

No significant difference was found in 1- and 5- year crude survival among hospitals with higher and lower resection rates when correcting for several tumor and patient characteristics. As

mentioned before, the postoperative mortality rate in colorectal cancer surgery remains substantial. Especially in the elderly a prolonged impact of surgery on survival is seen. Excess mortality sustains up to one year after surgery [6,22]. We found a 1-year mortality of nearly 20% for patients older than 75 years. This could explain why no difference was found in the 1-year crude survival between hospitals with high and low resection rates; in hospitals with the highest resection rates a higher mortality rate would be observed as a result of postoperative complications.

After 5 years however, no survival benefit was reported in patients treated in hospitals with the highest resection rates as compared to patients treated in hospitals with lowest resection rates. Also when assessing relative survival no significant excess risk of dying was observed among the four different groups. A possible explanation could be that the majority of patients who do not undergo surgery decease in the first year after diagnosis. But also when the same analysis was performed conditional on patients who survived the first year no difference was found. It is however important to mention that the overall resection rates observed in this study are high and the differences among hospitals may be too small to have a profound effect on survival.

A significant increase in resection rates of 93.3% in 2009–2010 to 94.6% in 2013–2014 was found in our study. This is in contrast to an earlier report by Speelman et al., which demonstrated a decrease in resection rate of different gastro-intestinal cancers [2]. This included a decline in resections of patients with colon cancer. It should be mentioned that their study population differed from ours since patients with metastatic disease and patients who underwent endoscopic resection were also included. Other factors may affect the rise in resection rates as well. Implementation of a national population screening program for bowel cancer that was launched in 2014 could have led to earlier detection of otherwise primarily non-resectable colon cancer. Besides, the increasing use of laparoscopy may also play a role. Moreover, some population demographics may have changed over time.

A limitation of this study is that it lacks information on comorbidities, frailty and patient preferences. A previous study by Kolfschoten et al. has demonstrated that high-risk patients are not evenly distributed among hospitals [23]. It is however important to mention that their study population only included patients that underwent surgery. Furthermore, although comorbidity could have influenced the probability of undergoing resection, comparable studies on the probability of receiving treatment for gastric or esophageal cancer revealed only slight changes in the probability of treatment after adjustment for comorbidity, indicating a minimal contribution of this factor to the observed variation in probabilities between hospitals of diagnosis [8,24]. Considering the outcome of the present study, it would be interesting to know if part of the difference they found was a result of patient selection rather than actual variation in casemix of the entire colon cancer population. This would imply differences in management and selection of colon cancer patients may have a more profound effect on surgical outcome than the variation in casemix that is corrected for by current audits [10].

In the Netherlands, patients are free to choose the hospital of preference since all hospitals performing colorectal cancer surgery are public. In general, patients visit the hospital that is closest to their home. Unfortunately, no information on patients preferences is registered in the NCR. It is therefore also unknown if and why patients decided to refrain from surgery themselves in the present study.

On the other hand, a strength of the current study is that besides overall survival, also relative survival was assessed, which represents a good estimate for disease-specific survival. Additionally, the nationwide approach and very high number of patients in the present study add to its strength.

In conclusion, there is a significant variation in resection rates in patients with non-metastatic colon cancer among hospitals in the Netherlands. This variation increases in the elderly. Nevertheless, no significant effect on survival was found. This could imply that undertreatment may play a role as well as that some patients might not benefit from surgery. The reasons for the variation in resection rates between hospitals need to be studied further.

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