CHAPTER 9

Safety of elective colorectal cancer surgery: non-surgical complications and colectomies are targets for quality improvement.

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ABSTRACT

Background: Mortality following severe complications (failure to rescue, FTR) is targeted in surgical quality improvement projects. Rates may differ between colon- and rectal cancer resections.

Methods: Analysis of patients undergoing elective colon and rectal cancer resections registered in the Dutch Surgical Colorectal Audit in 2011 – 2012. Severe complication- and FTR rates were compared between the groups in univariate and multivariate analysis.

Results: Colon cancer (CC) patients (n=10184) were older and had more comorbidity. Rectal cancer (RC) patients (n=4906) less often received an anastomosis and had more diverting stomas. Complication rates were higher in RC patients (24.8% vs. 18.3%, P<0.001). However, FTR rates were higher in CC patients (18.6% vs 9.4% p<0.001). Particularly, FTR associated with anastomotic leakage, postoperative bleeding and infections was higher in CC patients. Adjusted for casemix, CC patients had a two-fold risk of FTR compared to RC patients (OR 1.89, 95% CI 1.06-3.37).

Conclusions: Severe complication rates were lower in CC patients than in RC patients; however, the risk of dying following a severe complication was twice as high in CC patients, regardless of differences in characteristics between the groups. Efforts should be made to improve recognition and management of postoperative (non-)surgical complications, especially in colon cancer surgery.

INTRODUCTION

Ever since the Institute of Medicines report 'to err is human', patient safety is a number one priority in many western health care systems. Colorectal cancer surgery is performed commonly, though it remains associated with relatively high morbidity and mortality rates[1,2], in part because colorectal cancer patients often have a high age and comorbid illnesses[3]. As a result, colorectal cancer surgery is the subject of many national quality improvement programs in Europe[4] and the United States[5], with complication- and mortality rates being widely used outcomes for comparisons of quality of surgical care. *Failure to rescue (FTR)* - the mortality rate in patients with a severe complication - is another outcome measure that indicates the ability of a surgical team to keep patients alive when severe complications occur[6-8]. FTR is seen as a good quality indicator as it evaluates both complication recognition and treatment.

Following the example of audits in other European countries, the nationwide Dutch Surgical Colorectal Audit (DSCA) was introduced in the Netherlands in 2009[9]. One of the main objectives of these audit programs is to reduce morbidity and mortality after colorectal surgery. To reach this objective, it is important to understand the mechanisms behind the development of adverse events and the way they lead to fatal outcomes. In the DSCA, postoperative mortality appears to be higher after colon cancer resections than after rectal cancer resections, despite higher complication rates in the latter[9], suggesting higher FTR rates in colon cancer surgery. These differences in FTR may be partly due to a higher proportion of non-elective surgery in colon cancer patients, which carries a higher risk of adverse events[10], though may also exist in elective cases. A similar pattern was observed in the British National Bowel Cancer Audit Program, with higher postoperative mortality rates after colon resections than

after rectal cancer resections, both in elective and non-elective cases, despite higher reoperation rates in rectal cancer patients[11].

Differences in patient characteristics, such as age, comorbidity, and tumor stage between colon and rectal cancer patients may also play a role in the differences in outcomes between the two patient groups. Moreover, possible differences in treatment characteristics, such as neoadjuvant therapy, fecal diversion and minimally invasive surgery may play a role.

The purpose of this study was to evaluate differences in FTR rates between elective colon and rectal cancer resections in relation to the characteristics of these patient groups and differences in treatment patterns between colon and rectal cancer patients.

PATIENTS AND METHODS

Data source

A retrospective review of prospectively collected clinical data was undertaken. Data were provided by the DSCA, a national quality improvement project in which all hospitals performing colorectal cancer surgery participate and in which a variety of characteristics concerning patient demographics, comorbidity, diagnostics, disease-specific details, treatment and outcomes are collected prospectively. Inclusion criteria for registration are patients undergoing a resection for primary colorectal cancer. External data verification with the dataset of the Netherlands Cancer Registry (NCR), showed a 95% case-ascertainment of the DSCA in 2011[9] which increased to 97% in 2012[12].

Patients

For this study, no ethical approval was required under Dutch law. Patients undergoing any surgical resection for primary colorectal cancer between the 1st of January 2011 and 31st of December 2012, and registered in the DSCA before March 15th 2013, were evaluated. Minimal data requirements to consider a patient eligible for analyses were information on tumor location, date of surgery, complications and mortality. Patients undergoing non-elective surgery were excluded since these patients represent a subgroup of patients with other treatment perspectives and subsequent different expected outcomes[13]. Finally, patients treated for multiple synchronous colorectal tumors were excluded to make sure a clear distinction between colon and rectal cancer patients could be made.

Outcomes

Postoperative complications were defined as all surgical or non-surgical postoperative complications. In the DSCA, surgical complications (e.g. anastomotic leak, hemorrhage) are only registered when a reintervention was performed.

Failure to rescue was, in accordance with previous publications, defined as the mortality rate among patients with a severe complication[8,14]. Severe complications were defined as complications leading to ICU admission (longer than 2 days), to a reintervention, to a prolonged hospital stay of more than 14 days, or to postoperative mortality. This is consistent with previous publications in which data from the DSCA were analyzed[8,15], except for the ICU criterion which was added for a more precise characterization of severe complications. The reason this criterion was not used in previous publications is that data on ICU admission were lacking from the DSCA database before 2011. Patients with a prolonged hospital stay, in which no

complication was registered, were not included in the definition of a severe complication.

Anastomotic leakage was defined as clinically apparent leakage or an abscess in the proximity of the anastomosis. Intra-abdominal abscesses were registered as such when not evidently associated with anastomotic leakage. Infectious/septic complications were all infections not meeting other (pulmonary, urinary tract, intra-abdominal etc.) criteria, for instance central venous catheter related infections, or wound infections.

Postoperative mortality was defined as death within 30 days from surgery or within the same hospital admission as the resection.

Statistical analysis

Categorical variables were compared between colon cancer and rectal cancer patients by Chi-square tests, while 2-sample t tests were used for continuous variables.

The risk of FTR after severe complications, adjusted for patient- and tumor related risk factors, was calculated with multivariable logistic regression with addition of patient category (colon or rectal cancer patients) as a variable in the model. A random effects model adjusted for the presence of variability in outcomes between hospitals.

To assess whether differences in hospital characteristics of hospitals treating colon- and rectal cancer patients influenced differences in outcomes between colon- and rectal cancer patients, we repeated our analysis in a fixed effects model with the addition of the variables teaching status, hospital volume, and level of ICU facilities according to a previous study[14].

A 2-sided $P \leq 0.05$ was considered statistically significant. Statistical analyses were performed in PASW Statistics version 20 (SPSS inc., Chicago, Il, USA) and R 2-14 (The R Project for Statistical Com-

puting and The Comprehensive R Archive Network; http://cran.r-project.org/).

RESULTS

Patients

A total of 15,090 patients undergoing elective colon or rectal cancer resections in 92 hospitals were included. Patient characteristics are displayed in table 1.

Colon cancer patients were less often male, were older and had higher Charlson comorbidity scores and ASA classifications compared to rectal cancer patients. TNM stage was also higher in colon cancer patients. A primary anastomosis was constructed less often in rectal cancer patients, with more often fecal diversion in case of an anastomosis, compared to colon cancer patients. Laparoscopic resection rates were quite similar in both patient groups.

Outcomes

The overall postoperative complication and reintervention rates were lower in colon cancer patients than in rectal cancer patients. Median length of stay was one day longer in rectal cancer patients with a higher proportion of patients with a length of stay longer than 14 days compared to colon cancer patients. Duration of postoperative ICU admission did not differ much between colon and rectal cancer patients.

Severe complication (see definitions in the methods section) rates were higher in rectal cancer patients than in colon cancer patients ($p<0.001$) (table 2). Colon cancer patients with a severe complication met the ICU criterion more often. The majority of colon and rectal cancer patients with a severe complication had a prolonged hospital

Table 1: Patient characteristics of colon and rectal cancer patients.

Patient characteristics		Colon cancer		Rectal cancer		p for difference
Number of patients		10184		4906		.
Gender	male	5299	52%	1596	63%	p<0.001
Age	mean, standard deviation	71	11	67	11	p<0.001
Body mass index	mean, standard deviation	26,3	4,5	26,2	4,3	n.s.
Charlson comorbidity score	charlson 0	4979	48,9%	2837	57,8%	p<0.001
	charlson 1	2445	24,0%	1058	21,6%	
	charlson 2	1572	15,4%	609	12,4%	
	charlson 3 or higher	1189	11,7%	402	8,2%	
ASA classification	I	1961	19,3%	1271	25,9%	p<0.001
	II	5834	57,3%	2826	57,6%	
	III or higher	2366	23,2%	802	16,3%	
	unknown	23	0,2%	6	0,1%	
TNM stage	X	100	1,0%	22	0,4%	p<0.001
	I	2229	21,9%	1879	38,3%	
	II	3719	36,5%	1224	24,9%	
	III	3107	30,5%	1444	29,4%	
	IV	1029	10,1%	337	6,9%	

Table 1: Patient characteristics of colon and rectal cancer patients. (continued)

Patient characteristics		Colon cancer		Rectal cancer		p for difference
Number of patients		10184		4906		.
Procedure	Ileocecal resection	111	1,1%	.	.	.
	Right hemicolectomy	4741	46,6%	.	.	
	transverse colectomy	293	2,9%	.	.	
	left hemicolectomy	971	9,5%	.	.	
	sigmoid colectomy	3819	37,5%	.	.	
	Low anterior resection	.	.	3334	68,0%	
	Subtotal colectomy / panproctocolectomy	184	1,8%	33	0,7%	
	Abdominoperineal resection	.	.	1463	29,8%	
	Other	55	0,5%	75	1,5%	
Approach	laparoscopic	5396	53,0%	2511	51,2%	n.s.
Anastomosis	primary anastomosis	9022	88,6%	745	15,2%	p<0.001
	anastomosis with defunctioning stoma	389	3,8%	1709	34,8%	
	no anastomosis	581	5,7%	2280	46,5%	

N.s.=not significant

Table 2: Outcomes in colon and rectal cancer patients.

	Colon cancer		Rectal cancer	
	n (patients)	%	n (patients)	%
Any complication	2760	27.4%*	1775	36.5%*
Reintervention	1075	10.6%*	687	14.0%*
Length of stay				
Median	7 days		8 days	
>14 days	1553	15.4%*	1075	22.1%*
ICU admission				
0-1 day	8624	84.7%*	4121	84.0%*
2 days	328	3.2%*	213	4.3%*
3-7 days	405	4.0%*	196	4.0%*
8-14 days	150	1.5%*	58	1.2%*
> 14 days	138	1.4%*	53	1.1%*
unknown	539	5.3%*	265	5.4%*
Severe complication	1863	18,3%*	1218	24,8%*
Reason:				
Postoperative mortality	347	18,6%**	114	9,4%**
ICU admission > 2 d	693	37,2%**	307	25,2%**
Reintervention	1075	57,7%**	687	56,4%**
Complication + hospital stay >14 d	1268	68,8%**	834	68,5%**
Number of severe complications				
1	1217	12.0%*	902	18.4%*
2	437	4.3%*	221	4.5%*
3	164	1.6%*	73	1.5%*
4 or more	44	0.4%*	22	0.4%*
Failure to rescue	347	18,6%**	114	9,4%**
Postoperative mortality		3,4%*		2,3%*

*percentage of all patients ** percentage of all patients with a severe complication. Note that patients may have met multiple criteria for a severe complication

Table 3: incidence of and failure to rescue (FTR) from serious complications, displayed per complication type. Note that patients may have had more than one complication and that numbers add up to more than the total.

	colon cancer		rectal cancer		
	severe complication	FTR (%)	severe complication	FTR (%)	p for difference
anastomotic leakage	576	72 (12,5%)	215	11 (5,1%)	p=0.003
intra-abdominal abscess	16	2 (12,5%)	80	3 (3,8%)	n.s.
postoperative bleeding	51	11 (21,6%)	35	1 (2,9%)	p=0.014
ileus	84	9 (10,7%)	84	3 (3,6%)	n.s.
fascial dehiscence	105	7 (6,7%)	59	4 (6,8%)	n.s.
pulmonary complication	448	115 (25,7%)	199	45 (22,6%)	n.s.
cardiac complication	262	97 (37%)	111	31 (27,9%)	n.s.
infection/septic complication	235	49 (20,9%)	140	14 (10%)	p=0.007

stay but only in 20 and 27% of patients with a severe complication, respectively, a prolonged hospital stay following a complication was the sole reason for inclusion in the severe complication group.

FTR from severe complications – the mortality rate among the patients defined as having a severe complication – was higher in colon cancer patients, resulting in a higher overall postoperative mortality rate in colon cancer patients ($p<0.001$ for both outcomes).

Table 3 shows the most important severe complications for colon and rectal cancer patients. In colon cancer patients, the most frequent complications were anastomotic leakage (5.6% of all colon cancer patients and 6.1% of colon cancer patients with an anastomosis), pulmonary complications (4.8%) and cardiac complications (2.6%). In rectal cancer patients, the most common severe complications were anastomotic leak (4.4% of all rectal cancer patients and 8.7% of rectal cancer patients with anastomosis), pulmonary complications (4.1%) and infections/septic complications (2.9%).

Overall, FTR from severe complications was highest in both patient groups when associated with pulmonary and cardiac complications. FTR was higher in colon cancer patients than in rectal cancer patients when associated with anastomotic leakage (12.5% vs 5.1% p=0.003), postoperative bleeding (21.6% vs. 2.9%, p=0.014) and infections/ septic complications (20.9% vs. 10.0%, p=0.007). FTR rates associated with other complication types were not significantly different between the two patient groups.

Most patients had one severe complication, but some had several (table 2). FTR rates increased with the number of severe complications that a patient experienced postoperatively. In colon cancer patients this increased from 15.7% in patients that had one severe complication to 36.4% in patients that experienced four or more

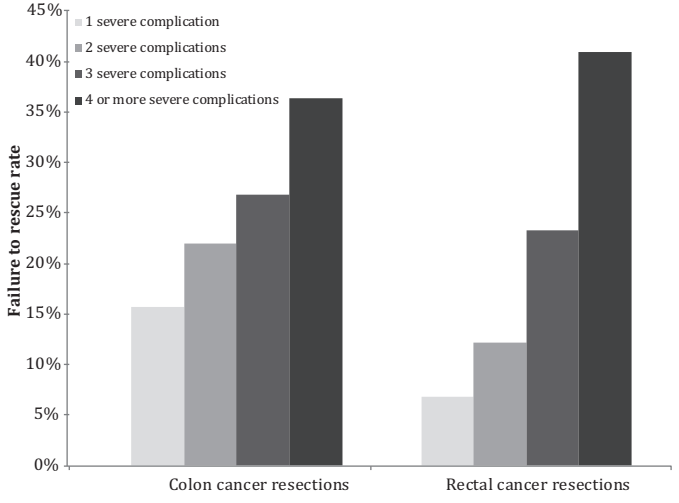

Figure 1: Failure to rescue rates according to the number of severe complications

Table 4: Multivariate analysis for the risk of failure to rescue in patients with a severe complication.

Variable		Odds Ratio	95% CI
Gender	male	1	ref
	female	0.84	0.66-1.08
Age	<=70 years	1	ref
	>70 years	**2.86**	**2.09-3.89**
Body mass index	<20	1.06	0.64 -1.74
	20-24.9	1	ref
	25-29.9	**0.75**	**0.57-0.98**
	30 or higher	**0.71**	**0.50-0.99**
Charlson comorbidity score	0	1	ref
	1	**1.42**	**1.03-1.95**
	2	1.03	0.71-1.48
	3 or higher	**1.97**	**1.38-2.82**
ASA classification	I	1	ref
	II	**1.97**	**1.51-2.58**
	III or higher	**4.07**	**2.26-7.32**
TNM stage	I	1	ref
	II	0.87	0.64-1.19
	III	0.94	0.86-1.31
	IV	1.23	0.79-1.92
Neoadjuvant therapy	none	1	ref
	short course RT	1.28	0.71-2.31
	chemoradiotherapy	0.80	0.40 -1.60
Approach	open	1	ref
	laparoscopic	1.04	0.80 -1.36
Additional resections	none	1	ref
	limited*	0.89	0.50 – 1.58
	extensive**	0.94	0.56 – 1.58
Anastomosis	primary anastomosis	1	ref
	anastomosis with defunctioning stoma	0.74	0.47 -1.17
	no anastomosis	1.07	0.74-1.55
Resection type	rectal cancer resection	1	ref
	colon cancer resection	**1.89**	**1.06-3.37**

ASA=American Society of Anesthesiologists CI=confidence interval. Bold printed numbers are significant associations (P<0.05). *abdominal wall, omentum, posterior vaginal wall, ovaries. **organ resection (pancreas, small bowel, spleen, kidney, liver, stomach, sacrum, bladder/urethra/ureters/prostate, uterus)

severe complications. In rectal cancer patients this increased from 6.8% to 41% (figure 1).

Risk factors

Table 4 displays the results of the multivariable regression analysis for the association between patient-, tumor-, and treatment factors and the association with FTR in patients who had a severe complication. Adjusted for these variables, colon cancer patients had an almost two-fold higher risk of dying secondary to a severe complication than rectal cancer patients.

Other independent predictors of FTR were advanced age and higher Charlson comorbidity and ASA scores. Higher body mass index was associated with a lower risk of FTR. Gender, neoadjuvant therapy, additional organ resections, laparoscopic resections and stoma construction were not significantly associated with outcome.

In a repeated analysis with adjustment for the hospital characteristics in the model, the difference in FTR between colon and rectal cancer patients remained the same (colon vs. rectal cancer resection: adjusted OR 1.88; 95% CI 1.04 – 3.39). There was no significant effect of volume or teaching status on FTR rates but better ICU facilities were associated with better FTR rates (level 2 vs. level 1; OR 0.54, 95% CI 0.35 – 0. 84 and level 3 vs. level 1; OR 0.83, 95% CI 0.53 – 1.31).

DISCUSSION

This is the first study comparing FTR rates between patients undergoing a resection for colon cancer and rectal cancer. FTR was higher in colon cancer patients than in rectal cancer patients. This was partly because colon cancer patients were older, and had more comorbidity

and higher ASA classifications; although adjusted for the differences in patient- and treatment characteristics, the risk of FTR remained twice as high in colon cancer patients.

Schilling et al. described that colectomies account for a disproportionate share of morbidity, mortality and excess length of stay among all general surgical procedures. Colectomies account for 24% of all adverse events in general surgery with an adverse event rate of 29%[1]. In a Dutch study with data from the Eindhoven Cancer registry, it was shown that patient characteristics differ between colon- and rectal cancer patients, and that rectal cancer patients have a higher risk of postoperative complications, even though they are younger and less often have comorbid diseases than colon cancer patients[3]. Our study confirms the relatively high adverse event rate in colorectal surgery, and confirms that this rate is higher in rectal cancer surgery than in colon cancer surgery. Our study adds that the risk of dying given a severe complication is higher following a colon cancer resection than after a rectal cancer resection, even after adjustment for other relevant factors. Due to the nature of the database, our study provides a realistic image of outcomes of everyday practice in elective colorectal cancer surgery in the Netherlands.

Our study has some limitations. Firstly, as data are self-reported, registration bias cannot be excluded. However the dataset is validated against the independently collected data of the Netherlands Cancer Registry, showing a high rate of case-ascertainment, completeness and accuracy[12]. The direct involvement of clinicians in the registration leads to a robust database and avoids coding problems that may occur when using an administrative database. Secondly, although the definition of a severe complication we used is arbitrary, it excludes the less severe complications that did not hinder the postoperative course. Since ICU admission, reinterventions and prolonged hospital stay are objective criteria, FTR rates are not influenced by differences

in the way hospitals register minor complications. However, it cannot be excluded that some patients with a serious complication were not included in the definition. All (complications leading to) mortality cases were considered severe complications, regardless of reinterventions, ICU admission or prolonged hospital stay. We performed a sub analysis in only those patients who underwent a reintervention, had ICU admission or a complication with a prolonged hospital stay, and the difference in FTR rates between rectal and colon cancer patients remained the same (adjusted OR 2.1; 95% CI 1.06-4.37). Finally, with regards to the analysis of FTR rates associated with different complication types, we cannot exclude that patients who were registered as having experienced non-surgical complications might also have had undiscovered underlying surgical complications.

Anastomotic leakage is considered the most dreadful complication in colorectal surgery and accounts for a large proportion of overall postoperative mortality[16]. Indeed, in our study anastomotic leak was the most common severe complication. The proportion of leaks that lead to mortality was significantly higher in colon cancer patients, although the anastomotic leak rate was higher in rectal cancer patients (given an anastomosis was constructed). A part of the explanation may be found in the larger proportion of anastomoses with a defunctioning stoma in rectal cancer patients compared to colon cancer patients. Also, a large proportion of rectal cancer patients did not receive a primary anastomosis, and therefore the group of colon cancer patients was a priori more susceptible for mortality following anastomotic leak as well as possible associated non-surgical complications. However, diverting stomas and end-colostomies were not significantly associated with FTR. Moreover, adjusted for stoma rates, FTR remained higher in colon cancer patients. Early recognition and treatment of anastomotic leak may be associated with lower mortality associated with leakage[17]. Arguably, as the anastomosis

following rectal resections lies in the pelvic region, anastomotic leaks following rectal cancer resections often will have a more chronic course, developing a presacral sinus or pelvic abscess[18], whereas colonic anastomotic leaks might have a higher risk of fecal peritonitis due to the intra-abdominal location. Whether a longer delay or a more fulminant course of anastomotic leak in colon cancer patients has contributed to the differences in FTR between the two patients groups cannot be retrieved from the DSCA dataset, but should be the focus of future in-depth studies as a reduction in delay of diagnosing anastomotic leak may prove a potential target for improvement[19].

Cone et al. reported a high risk of mortality following postoperative non-surgical complications such as pneumonia and renal insufficiency in colorectal surgery patients[20]. Friese et al. described mortality rates and their relation with complications in 25,957 patients that underwent a surgical resection for colorectal- and other types of cancer[21]. Mortality was most frequently secondary to respiratory compromise (37% of postoperative mortality) and pneumonia (26%). Our study confirms that cardiopulmonary complications are often associated with postoperative mortality, although it is not possible to make a clear distinction between surgical and non-surgical complications as surgical complications may start a chain of non-surgical adverse events, leading to clinical deterioration and eventually death. It does however underline the importance of a high postoperative vigilance for non-surgical complications besides the intuitively important surgical complications such as anastomotic leak. Aggressive, multidisciplinary treatment of complications such as pneumonia, arrhythmias or central venous catheter sepsis may prevent postoperative death from non-surgical complications. Arguably, adequate preoperative optimization of the patient's condition may be an even more important step in reducing mortality from non-surgical complications. Fuchshuber et al. describe how a hospital drastically improved the

number of patients on a ventilator for >48 hours, and achieved a zero postoperative pneumonia rate in patients undergoing thoracoabdominal surgery during seven months by strictly adhering to a few perioperative steps[22]. Similar achievements have been published about reducing the number of acute bloodstream infections related to central venous catheters[23]. A recent meta-analysis showed that measuring the C-reactive protein on postoperative day 4 has a pooled negative predictive value of 89% for predicting postoperative infectious complications after colorectal surgery, allowing safe discharge of patients not at risk[24].

In the last decade, improvement of clinical outcomes for complex, low-volume gastrointestinal cancer surgery such as pancreatic, esophageal and rectal cancer resections has received much attention in the western world[25-30]. In the Netherlands, specialization of caregivers, focused improvements to infrastructure, specific interventions to perioperative management and selective referral have led to dramatic improvements in outcomes of patients undergoing these particular procedures[31-35]. In contrast, CC surgery received less attention and is, as a result, often performed in a non-focused setting. In a previous study, we found no association between FTR and hospital volume or teaching status in colorectal cancer patients, but better FTR rates in patients operated in hospitals with better ICU facilities[14]. We therefore repeated our analyses including these hospital characteristics, confirming the association between ICU facilities and FTR rates. However, the difference in FTR between colon and rectal cancer patients remained the same in this second analysis and we cannot conclude that the difference in FTR between colon and rectal cancer patients can be attributed to differences in hospital characteristics in which colon- and rectal cancer patients are treated. Surgeons' differentiation may play a role- rectal cancer resections are usually performed by specialized gastrointestinal surgeons,

whereas colon cancer resections are often performed by surgeons without gastrointestinal specialization- but our study has no data on a surgeon level to support this. Recently, the Association of Surgeons of the Netherlands started with certification of surgeons performing colon cancer procedures.

In conclusion, the incidence of severe postoperative complications was lower in colon cancer patients than in rectal cancer patients; however, the risk of dying when a severe complication had occurred (FTR) was twice as high in colon cancer patients, even after adjustment for differences in patient-, tumor-, and treatment characteristics between the two patient groups. In particular, FTR associated with anastomotic leak, postoperative bleeding and non-surgical infectious complications was higher in colon cancer patients than in rectal cancer patients. Given the results of our study, efforts should be made to improve recognition and management of postoperative surgical and non-surgical complications in order to reduce postoperative mortality. Especially patients undergoing colon cancer surgery should receive full attention.

REFERENCES

1. Schilling PL, Dimick JB, Birkmeyer JD. Prioritizing quality improvement in general surgery. J Am Coll Surg 2008;207:698-704.
2. Dimick JB, Welch HG. The zero mortality paradox in surgery. J Am Coll Surg 2008;206:13-6.
3. Lemmens VE, Janssen-Heijnen ML, Houterman S, et al. Which comorbid conditions predict complications after surgery for colorectal cancer? World J Surg 2007;31:192-9.
4. van Gijn W, Wouters MW, Peeters KC, van de Velde CJ. Nationwide outcome registrations to improve quality of care in rectal surgery. An initiative of the European Society of Surgical Oncology. J Surg Oncol 2009;99:491-6.
5. Ingraham AM, Richards KE, Hall BL, Ko CY. Quality improvement in surgery: the American College of Surgeons National Surgical Quality Improvement Program approach. Adv Surg 2010;44:251-67.
6. Silber JH, Rosenbaum PR, Schwartz JS, Ross RN, Williams SV. Evaluation of the complication rate as a measure of quality of care in coronary artery bypass graft surgery. JAMA 1995; 274:317-23.
7. Ghaferi AA, Birkmeyer JD, Dimick JB. Variation in hospital mortality associated with inpatient surgery. N Engl J Med 2009;361:1368-75.
8. Henneman D, Snijders HS, Fiocco M, et al. Hospital Variation in Failure to Rescue after Colorectal Cancer Surgery: Results of the Dutch Surgical Colorectal Audit. 2013;20(7): 2117-23.
9. Van Leersum NJ, Snijders HS, Henneman D, et al. The Dutch Surgical Colorectal Audit. Eur J Surg Oncol 2013;39(10):1063-70.
10. Kolfschoten NE, Wouters MW, Gooiker GA, et al. Nonelective colon cancer resections in elderly patients: results from the dutch surgical colorectal audit. Dig Surg 2012;29:412-9.
11. National Bowel Cancer Audit Program. Annual Report. www.ic.nhs.uk/bowel; 2012. Accessed 01-09-2013
12. Dutch Institute for Clinical Auditing Annual Report 2012. http://www.clinicalaudit.nl; 2013. Accessed 01-09-2013
13. Kolfschoten NE, Wouters MW, Gooiker GA, et al. Nonelective Colon Cancer Resections in Elderly Patients: Results from the Dutch Surgical Colorectal Audit. Dig Surg 2012;29:412-9.
14. Henneman D, van Leersum NJ, Ten Berge M, et al. Failure-to-Rescue After Colorectal Cancer Surgery and the Association with Three Structural Hospital Factors. Ann Surg Oncol 2013; 20(11):3370-6.

15. Kolfschoten NE, van Leersum NJ, Gooiker GA, et al. Successful and Safe Introduction of Laparoscopic Colorectal Cancer Surgery in Dutch hospitals. Ann Surg 2013.;257(5):916-21.

16. Snijders HS, Wouters MW, van Leersum NJ, et al. Meta-analysis of the risk for anastomotic leakage, the postoperative mortality caused by leakage in relation to the overall postoperative mortality. Eur J Surg Oncol 2012;38:1013-9.

17. Alves A, Panis Y, Pocard M, Regimbeau JM, Valleur P. Management of anastomotic leakage after nondiverted large bowel resection. J Am Coll Surg 1999;189:554-9.

18. Sloothaak DA, Buskens CJ, Bemelman WA, Tanis PJ. Treatment of chronic presacral sinus after low anterior resection. Colorectal Dis 2013 Jun;15(6):727-32

19. den Dulk M, Noter SL, Hendriks ER, et al. Improved diagnosis and treatment of anastomotic leakage after colorectal surgery. Eur J Surg Oncol 2009;35:420-6.

20. Cone MM, Herzig DO, Diggs BS, Rea JD, Hardiman KM, Lu KC. Effect of Surgical Approach on 30-Day Mortality and Morbidity After Elective Colectomy: a NSQIP Study. J Gastrointest Surg 2012;16:1212-7.

21. Friese CR, Earle CC, Silber JH, Aiken LH. Hospital characteristics, clinical severity, and outcomes for surgical oncology patients. Surgery 2010;147:602-9.

22. Fuchshuber PR, Greif W, Tidwell CR, et al. The power of the national surgical quality improvement program-achieving a zero pneumonia rate in general surgery patients. Perm J 2012;16:39-45.

23. Pronovost P. Interventions to decrease catheter-related bloodstream infections in the ICU: the Keystone Intensive Care Unit Project. Am J Infect Control 2008;36:S171 e1-5.

24. Warschkow R, Beutner U, Steffen T, et al. Safe and early discharge after colorectal surgery due to C-reactive protein: a diagnostic meta-analysis of 1832 patients. Ann Surg 2012;256: 245-50.

25. Tol JA, van Gulik TM, Busch OR, Gouma DJ. Centralization of Highly Complex Low-Volume Procedures in Upper Gastrointestinal Surgery. A Summary of Systematic Reviews and Meta-Analyses. Dig Surg 2012;29:374-83.

26. Hohenberger W, Merkel S, Hermanek P. Volume and outcome in rectal cancer surgery: the importance of quality management. Int J Colorectal Dis 2013;28:197-206.

27. Burke JP, Coffey JC, Boyle E, Keane F, McNamara DA. Early Outcomes for Rectal Cancer Surgery in the Republic of Ireland Following a National Centralization Program. Ann Surg Oncol 2013 Oct;20(11):3414-21

28. Allareddy V, Ward MM, Allareddy V, Konety BR. Effect of meeting Leapfrog volume thresholds on complication rates following complex surgical procedures. Ann Surg 2010;251: 377-83.

29. Dikken JL, van Sandick JW, Allum WH, et al. Differences in outcomes of oesophageal and gastric cancer surgery across Europe. Br J Surg 2013;100(1):83-94

30. Dimick JB, Pronovost PJ, Cowan JA, Lipsett PA. Surgical volume and quality of care for esophageal resection: do high-volume hospitals have fewer complications? Ann Thorac Surg 2003;75:337-41.

31. de Wilde RF, Besselink MG, van der Tweel I, et al. Impact of nationwide centralization of pancreaticoduodenectomy on hospital mortality. Br J Surg 2012;99:404-10.

32. Gooiker GA, van der Geest LG, Wouters MW, et al. Quality improvement of pancreatic surgery by centralization in the western part of the Netherlands. Ann Surg Oncol 2011;18: 1821-9.

33. Wouters MW, Krijnen P, Le Cessie S, et al. Volume- or outcome-based referral to improve quality of care for esophageal cancer surgery in The Netherlands. J Surg Oncol 2009;99: 481-7.

34. den Dulk M, van de Velde CJ. Quality assurance in surgical oncology: the tale of the Dutch rectal cancer TME trial. J Surg Oncol 2008;97:5-7.

35. Dikken JL, Dassen AE, Lemmens VE, et al. Effect of hospital volume on postoperative mortality and survival after oesophageal and gastric cancer surgery in the Netherlands between 1989 and 2009. Eur J Cancer 2012;48:1004-13.