Locally Advanced Colon Cancer: Evaluation of Current Clinical Practice and Treatment Outcomes at the Population Level

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Abstract

Background: The goal of this study was to evaluate current clinical practice and treatment outcomes regarding locally advanced colon cancer (LACC) at the population level. **Methods:** Data were used from the Dutch Surgical Colorectal Audit from 2009 to 2014. A total of 34,527 patients underwent resection for non-LACC and 6,918 for LACC, which was defined as cT4 and/or pT4 stage. LACC was divided into those with multivisceral resection (LACC-MV; n=3,385) and without (LACC-noMV; n=1,595). Guideline adherence, treatment strategy, and short-term outcomes were evaluated. **Results:** Guideline adherence was >90% regarding preoperative imaging and ≥80% regarding preoperative multidisciplinary team (MDT) discussion. In the elective setting, neoadjuvant chemoradiotherapy (chemoRT) was applied in 6.2% of the cT4 cases, and neoadjuvant chemotherapy in 4.0%. R0 resection rates were 99%, 91%, and 87% in patients with non-LACC, LACC-noMV, and LACC-MV, respectively ($P<.001$). A postoperative complicated course occurred in 17%, 25%, and 29% of patients ($P<.001$), and the 30-day/in-hospital mortality rate was 3.6%, 6.0%, and 5.4% ($P<.001$) in the non-LACC, LACC-noMV, and LACC-MV groups, respectively. **Discussion/Conclusions:** This population-based study suggests that there is room for improvement in the treatment of LACC, with regard to short-term surgical outcomes and oncologic outcomes (ie, radicality of resection). Improvement might be expected from optimized preoperative imaging, routine MDT discussions, and further specialization and centralization of care. Optimized use of neoadjuvant treatment strategies based on already available and upcoming evidence is likely to result in a better margin status and thereby a better long-term prognosis. Furthermore, lower R0 resection rates in an emergency setting suggest a potential role for bridging strategies in order to enable optimal staging, neoadjuvant treatment, and elective surgery by a surgical team most optimally qualified for the procedure.

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Background

Colon cancer is highly prevalent worldwide¹ and a major public health problem. A substantial group of patients (10%–15%) presents with locally advanced colon cancer (LACC), which has an important impact on disease management and prognosis. Standard curative-intent treatment of LACC is a complete resection of the tumor (R0 resection)^{2,3} followed by

adjuvant systemic chemotherapy, depending on the age and clinical condition of the patient.

LACC can be subdivided into T4a stage with serosal ingrowth and T4b stage with ingrowth into nearby tissues or organs.⁴ In order to achieve a R0 resection of T4b tumors, the surgical approach should include a multivisceral resection with or without neoadjuvant downstaging.^{5,6} Despite the prevalence of LACC and its

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relatively poor prognosis, treatment of LACC is still an underexposed area in the field of colorectal cancer (CRC) care when compared with, for example, the extensive literature on locally advanced rectal cancer.

The Dutch Surgical Colorectal Audit (DSCA) has been evaluating and reporting on the quality of care of primary CRC surgery since 2009.^{7,8} The goal of this study was to evaluate current clinical practice regarding and short-term outcomes of the treatment of LACC at the population level using DSCA data.

Methods

Data Set

Data were derived from the DSCA, a disease-specific national audit. The audit collects information on patients, tumors, treatment characteristics, and outcomes and contains data from approximately 97% of all patients who underwent resection for primary CRC in the Netherlands. Data entry is obligatory and data are stored in a highly secured online database. All 92 Dutch hospitals participate and appoint a surgeon responsible for data entry. The data set is cross-checked several times with data registered in the Netherlands Cancer Registry to ensure completeness. Detailed information on the validity, collection, and methodology of the data set was published previously.^{7,8}

Patients

For this study, no ethical approval or informed consent was required under Dutch law. All patients who underwent surgery between January 1, 2009, and December 31, 2014, and were registered before March 15, 2015, were evaluated. Patients with multiple synchronous tumors within the colon were included, but patients with a second tumor in the rectum were excluded. Patients were considered eligible for this study if at least the following data were available: tumor location, date of surgery, and survival status at the time of hospital discharge. Based on these criteria, 98.7% (n=39,491) of all registered patients were available for analysis. Furthermore, for the purpose of the present analysis, all patients with metastatic disease were excluded.

Definitions

In the DSCA, both clinical and pathologic T stage were available, but without subdivision in T4a

and T4b. LACC was defined as all patients with a registered clinical and/or pathologic T4 stage. The extent of surgery for the primary tumor was registered in the DSCA as no, limited, or extensive additional resections for local ingrowth. Limited additional resections were defined as resections of the abdominal wall, omentum, or ovaries. Extensive additional resections referred to resections of the pancreas, spleen, kidney, liver, stomach, bladder, ureters, or uterus, or additional bowel resections. The organs involved or the exact locations of the additional resections are not specified. The variable additional resections for local ingrowth were used to define 2 subgroups: LACC without additional/multivisceral resections (LACC-noMV) and LACC with limited or extended additional/multivisceral resections (LACC-MV). All other colon cancer resections were referred to as non-LACC. In short, the following 3 subgroups were used in this study: LACC-noMV, which comprised patients who underwent a resection of a cT4 and/or pT4 colon carcinoma without the need for a multivisceral resection; LACC-MV, which comprised patients who underwent a multivisceral resection of a cT4 and/or pT4 colon carcinoma; and non-LACC, which comprised patients who underwent a resection for a T1–3 colon cancer (ie, a tumor not classified as either cT4 or pT4).

Emergency surgery was defined as surgery performed within 12 hours after the procedure was scheduled. Urgent surgery referred to semiurgent procedures that were scheduled >12 hours before being performed but outside of the elective program. The surgical approach was either open, laparoscopic, or converted laparoscopic surgery. Hospital volume was defined as the number of resections performed for LACC-MV per hospital per year.

Outcome variables were guideline adherence (guidelines are provided later), radicality of resection, and postoperative course. The subcategories for radicality of resections were R0, which denoted complete tumor resection with all margins histologically uninvolved; R1, which denoted incomplete resection with microscopic surgical resection margin involvement; and R2, which denoted incomplete tumor resection with gross residual tumor that was not resected. A complicated course referred to a postoperative complication leading to a reintervention, hospital stay >14 days, or

death. Surgical complications were directly related to the surgical procedure (ie, anastomotic leakage, abscess, bleeding, ileus). Nonsurgical complications were not directly related to the surgery (ie, postoperative pneumonia). Mortality was defined as 30-day or in-hospital mortality.

Treatment for LACC According to the Dutch Guidelines

The Dutch CRC guideline, which was used until June 2014, advised to routinely perform a preoperative CT scan for colon cancer. In the case of LACC, this was aimed at optimizing the surgical approach with en bloc multivisceral resection and at considering neoadjuvant therapy. Preoperative chemoradiotherapy (chemoRT) had to be considered if R0 resection was found to be unachievable based on CT imaging or intraoperative findings from an explorative laparotomy. Postoperative chemoRT had to be considered in cases of R2 resection with clipping of the operative field. In the revised guideline available April 2014 (www.oncoline.nl/colorectaalcarcinoom), preoperative imaging and multidisciplinary team (MDT) discussion were recommended in order to select the optimal treatment strategy. Preoperative systemic therapy is added as a neoadjuvant treatment option, besides chemoRT. Postoperative chemoRT for LACC is no longer advised ([see supplemental eAppendix 1, available with this article at JNCCN.org.](#)).

Statistical Analysis

Differences in baseline characteristics and outcome variables between patients with non-LACC, LACC-noMV, and LACC-MV were analyzed using a chi-square test or Fisher exact test in the case of categorical variables. The Kruskal-Wallis one-way analysis of variance was used for continuous (nonparametric) variables. R0 resection proportions were compared between different subgroups based on resection type, surgical approach, neoadjuvant treatment, and hospital volume. To determine potential improvement in quality of care over time, outcome parameters were plotted against year of registration. The trend over time was analyzed using the chi-square test for linearity. $P < .05$ was considered statistically significant. Statistical analyses were performed in PASW Statistics, version 22 (PASW Inc., Chicago, IL).

Results

Patients

Of all patients with colon cancer registered between January 1, 2009, and December 31, 2014, in 92 Dutch hospitals, 39,491 were eligible for analysis. A total of 4,964 patients were staged as M1 and excluded from this analysis. Clinical T stage was known in only 27% of the remaining 34,527 patients, and cT4 stage was registered in 578 patients. A total of 4,730 patients had a pathologic T4 tumor. There was an overlap between these groups in the case of 328 patients who had tumors classified as both cT4 and pT4, which resulted in a total of 4,980 patients with cT4 and/or pT4 stage disease (LACC); the remaining 29,547 (86%) were patients classified as non-LACC (Figure 1). In the LACC group, 3,385 patients (68%) were classified as LACC-noMV and 1,595 patients (32%) as LACC-MV. Limited and extensive additional resections were performed in 53% and 47% of the LACC-MV patients, respectively.

Baseline Characteristics and Surgery

Baseline characteristics of the 3 subgroups are outlined in Table 1. Compared with non-LACC patients, those with LACC-noMV and those with LACC-MV experienced more preoperative tumor complications (34% vs 51% and 52%, respectively). The percentage of procedures in the emergency/urgent setting was 14% for non-LACC and 33% and

Figure 1. Subdivision of patients into non-LACC, LACC-noMV and LACC-MV.

Abbreviations: DSCA, Dutch Surgical Colorectal Audit; LACC, locally advanced colon cancer; MV, multivisceral resection required; noMV, no multivisceral resection required; non-LACC, all other colon cancer resections.

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Table 1. Baseline Characteristics

	non-LACC		LACC-noMV		LACC-MV		χ^2
	n	%	n	%	n	%	
Sex							
Male	15,502	52%	1,669	49%	708	44%	<.001
Female	14,044	48%	1,716	51%	886	56%	
Age, y							
≤60	4,600	16%	526	15%	259	16%	.005
61–70	8,405	28%	939	28%	462	29%	
71–80	10,520	36%	1,140	34%	527	33%	
≥81	6,014	20%	780	23%	347	22%	
ASA score							
I–II	21,866	75%	2,357	71%	1,146	72%	<.001
III	6,844	23%	886	27%	408	26%	
IV–V	534	1.8%	98	2.9%	36	2.3%	
Preoperative complications caused by the tumor							
None	19,470	66%	1,658	49%	759	48%	<.001
Perforation with fecal peritonitis	334	1.1%	180	5.4%	69	4.4%	
Abscess	214	0.7%	90	2.7%	94	5.9%	
Obstruction	3,236	11%	805	24%	324	21%	
Blood loss/anemia	4,649	16%	419	13%	176	11%	
Other	1,416	4.8%	209	6.2%	162	10%	
Operative setting							
Elective (including after stent placement)	25,349	86%	2,250	67%	1,125	71%	<.001
Emergency/urgent	4,151	14%	1,132	33%	470	29%	
Pathologic N stage							
N0	19,328	66%	1,336	40%	847	54%	<.001
N1	6,733	23%	1,081	33%	436	28%	
N2	3,035	10%	907	27%	294	19%	
Nx	325		44		15		
Surgical approach							
Open	13,999	47%	2,175	64%	1,247	78%	<.001
Laparoscopic	13,587	46%	982	29%	166	10%	
Laparoscopic – converted	1,961	6.6%	228	6.7%	182	11%	
Surgical procedure							
Ileocecal resection	325	1.1%	61	1.8%	21	1.3%	<.001
(Extended) right hemicolectomy	13,316	45%	1,679	50%	677	42%	
Transverse resection	774	2.6%	79	2.3%	75	4.7%	
(Extended) left hemicolectomy	3,186	11%	383	11%	215	14%	
(Low) anterior/sigmoid resection	10,970	37%	1,038	31%	548	34%	
Subtotal colectomy	545	1.8%	77	2.3%	37	2.3%	
Panproctocolectomy	174	0.6%	10	0.3%	5	0.3%	
Other	257	0.9%	58	1.7%	17	1.1%	
Anastomosis							
Anastomosis	25,562	88%	2,611	79%	1,131	73%	<.001
Anastomosis with diverting ostomy	1,076	3.7%	144	4.3%	123	7.9%	
End ostomy	2,352	8.1%	567	17%	300	19%	

Abbreviations: ASA, American Society of Anesthesiologists; LACC, locally advanced colon cancer; MV, multivisceral resection required; noMV, no multivisceral resection required.

29% for LACC-noMV and LACC-MV patients, respectively. LACC was associated with a higher proportion of nodal positivity compared with non-LACC. Within the LACC group, nodal positivity was higher for LACC-noMV compared with LACC-MV (60% vs 47%).

The surgical procedure commenced laparoscopically in 53% of patients with non-LACC, in 36% of those with LACC-noMV, and in 21% of those with LACC-MV. Conversion rates were 13%, 19%, and 52%, respectively. The proportion of primary anastomoses was considerably lower in LACC-MV patients compared with LACC-noMV and non-LACC patients (Table 1).

Guideline Adherence

Preoperatively, an abdominal CT at the least was performed in 92% of patients with LACC-noMV and in 95% of those with LACC-MV (Table 2); percentages were slightly higher (94% and 96%, respectively) if emergency/urgent procedures are excluded. Regarding preoperative MDT discussion, 80% of LACC-noMV and 82% of LACC-MV patients undergoing elective surgery were discussed during an MDT meeting. Considering cT4 stage in the elective setting only, 6.2% (n=22) of patients with LACC (either no-MV or MV) received neoadjuvant chemoRT and 4.0% (n=14) neoadjuvant systemic therapy.

Outcome Variables

Compared with non-LACC, the overall R0 resection proportion was lower in patients with LACC (99% vs 90%, respectively) (Table 3). A higher proportion of R1/R2 resections was found for LACC-MV compared with LACC-noMV ($P<.001$), and in the elective setting only ($P<.001$). R0 resection proportions were significantly higher in the elective setting compared with the emergency and urgent settings for both LACC-noMV (93% vs 87%; $P<.001$) and LACC-MV (90% vs 81%; $P<.001$). In the LACC-noMV group, the R0 resection proportion was significantly lower in converted procedures than in laparoscopically completed resections (89% vs 96%; $P<.001$), although similar R0 resection proportions were found in the LACC-MV group (90% after conversion vs 93% after laparoscopy). The R0 resection proportions after any form of

neoadjuvant treatment did not significantly differ from the overall groups.

Table 4 displays data on the postoperative course. The length of stay was longest for the LACC-MV subgroup. Additionally, complications occurred most often in the LACC-MV group. The 30-day/in-hospital mortality rate was significantly higher for LACC compared with non-LACC (5.8% vs 3.6%; $P<.001$) with multivisceral resection showing no significant impact ($P=.606$) in patients with LACC (Table 4).

Table 2. Guideline Adherence

	LACC-noMV		LACC-MV	
	n	%	n	%
Elective, emergency, and urgent procedures				
Preoperative imaging ^a				
Abdomen				
None	93	2.8%	18	1.2%
Ultrasound	184	5.6%	61	3.9%
CT	2,912	89%	1,406	91%
MRI-liver ^b	31	0.9%	15	1.0%
PET/CT ^b	63	1.9%	47	3.0%
Thorax				
None	305	9.1%	86	5.5%
Chest x-ray	2,292	68%	1,062	68%
CT	694	21%	373	24%
PET/CT ^b	65	1.9%	47	3.0%
Elective procedures only				
Preoperative imaging ^a				
Abdomen				
None	18	0.8%	3	0.3%
Ultrasound	128	5.8%	44	4.0%
CT	1,982	90%	993	91%
MRI-liver ^b	26	1.2%	11	1.0%
PET/CT ^b	57	2.6%	40	3.7%
Thorax				
None	79	3.5%	30	2.7%
Chest x-ray	1,561	70%	740	67%
CT	538	24%	294	27%
PET-CT ^a	58	2.6%	39	3.5%
MDT	1,784	80%	919	82%
Elective procedures, cT4				
Neoadjuvant therapies				
Chemotherapy	2	1.1%	12	6.7%
ChemoRT	5	2.9%	17	9.5%

Abbreviations: chemoRT, chemoradiotherapy; LACC, locally advanced colon cancer; MDT, multidisciplinary team discussion; MV, multivisceral resection required; noMV, no multivisceral resection required.

^aIn the Dutch Surgical Colorectal Audit database, preoperative imaging is registered for the abdomen and thorax separately. The imaging modality is further specified for both compartments, and only the one with highest accuracy is registered in case of multiple modalities.

^bAnalyzed as fulfilling guideline recommendation for preoperative imaging.

Table 3. Radicality of Resection

	non-LACC		LACC-noMV		LACC-MV		χ^2
	n	%	n	%	n	%	
Overall							
R0	28,605	99%	2,981	91%	1,363	87%	<.001
R1	222	0.8%	190	5.8%	135	8.7%	
R2	51	0.2%	93	2.8%	62	4.0%	
Elective procedures							
R0	24,618	99%	2,040	93%	990	90%	<.001
R1	146	0.6%	95	4.3%	79	7.2%	
R2	32	0.1%	50	2.3%	29	2.6%	
Emergency/Urgent procedures							
R0	3,949	98%	938	87%	373	81%	<.001
R1	72	1.8%	95	8.8%	56	12%	
R2	18	0.4%	43	4.0%	33	7.1%	
Open							
R0	13,453	99%	1,855	89%	1,049	86%	<.001
R1	132	1.0%	142	6.8%	111	9.1%	
R2	32	0.2%	78	3.8%	57	4.7%	
Laparoscopic							
R0	13,257	99%	926	96%	153	93%	<.001
R1	65	0.5%	31	3.2%	10	6.1%	
R2	12	0.1%	7	0.7%	1	0.6%	
Laparoscopic – converted							
R0	1,895	98%	200	89%	161	90%	<.001
R1	25	1.3%	17	7.6%	14	7.8%	
R2	7	0.4%	8	3.6%	4	2.2%	
Neoadjuvant chemotherapy ^a							
R0			22	85%	47	92%	.429 ^b
R1			2	7.7%	3	5.9%	
R2			2	7.7%	1	2.0%	
Neoadjuvant (chemo)RT ^a							
R0			9	90%	40	83%	.321 ^b
R1			0	0.0%	6	13%	
R2			1	10%	2	4.2%	

Abbreviations: chemoRT, chemoradiotherapy; LACC, locally advanced colon cancer; MV, multivisceral resection required; noMV, no multivisceral resection required; R0, complete tumour resection with all margins histologically uninvolved; R1 incomplete resection with microscopic surgical resection margin involvement; R2, incomplete tumour resection with gross residual tumour that was not resected.

^aOnly elective procedures included.

^bAnalyzed using Fisher exact test.

Patients with LACC-MV were treated in all 92 hospitals. Based on the number of these patients that were treated, the hospitals were subdivided into low-volume (≤ 5 procedures annually) and high-volume (> 5 procedures annually). There were 82 low-volume hospitals (median volume, 2.3; range, 0.2–5.0) and 10 high-volume hospitals (median volume, 6.9; range, 5.2–8.2). The R0 resection proportion was 86% in low-volume hospitals compared with 91% in high-volume hospitals ($P=.024$).

When examining the development of the quality of surgical care throughout the years, a significantly positive trend in completeness of

resection, postoperative complicated course, and 30-day/in-hospital mortality could be observed in the non-LACC and LACC-noMV groups. These improvements were less clear (and nonsignificant) in the LACC-MV group (Figure 2).

Discussion

This population study reports on clinicopathologic characteristics, treatment strategy, and short-term outcomes after resection of M0 LACC in 4,980 patients, who composed 13% of the registered patients who underwent resection for colon cancer during a

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Table 4. Postoperative Course and Complications

	non-LACC		LACC-noMV		LACC-MV		χ^2
	n	%	n	%	n	%	
Median length of stay (IQR), days	7 (5–11)		8 (5–14)		10 (7–16)		<.001 ^a
Complicated course ^b	5,509	17%	837	25%	460	29%	<.001
Nonsurgical complications	3,859	13%	561	17%	254	16%	<.001
Surgical complications	3,698	13%	494	15%	290	18%	<.001
Surgical reintervention	2,816	9.5%	355	11%	185	12%	.007
Radiologic reintervention	270	0.9%	47	1.4%	40	2.5%	<.001
Mortality ^c	1,070	3.6%	201	6.0%	86	5.4%	<.001

Abbreviations: IQR, interquartile range; LACC, locally advanced colon cancer; MV, multivisceral resection required; noMV, no multivisceral resection required.

^aAnalyzed using Kruskal-Wallis one-way analysis of variance.

^bComplicated course: postoperative complication leading to a reintervention, hospital stay >14 days, or death.

^c30-day/in-hospital mortality.

6-year study period in the Netherlands. Only a small proportion of patients with LACC were treated with neoadjuvant chemoRT and/or radiotherapy. The overall R0 resection proportion was 90% in patients with LACC, with the lowest proportion being 81% for those who underwent a multivisceral resection in a nonelective setting. Patients with LACC had a slightly worse postoperative outcome compared with non-LACC patients. Short-term outcomes improved over time for the LACC-noMV group, with the R0 resection proportion exceeding 95%. For the LACC-MV group, improvement over time was less clear and the R0 resection proportion in 2014 was 88%.

An R1 resection of a primary colon cancer has a strong and stage-independent negative prognostic impact on the survival and recurrence rate.⁹ In a recent single-institution cohort study, recurrence rates were 56% and 19% for R1 and R0 resection, respectively, with corresponding 5-year survival rates of 25% and 60%.¹⁰ Similar to our findings, the risk of incomplete resection was related to the T stage. R0 resection proportions were remarkably low: 65% for T4a and 50% for T4b. Another population-based study reported a 75% R0 resection proportion in 861 patients with T4a stage colon cancer.¹¹ These data and our findings suggest that there is room for improvement in surgery for LACC. This will have a positive impact on prognosis given its independent association with recurrence and survival. Furthermore, the 5.8% postoperative mortality rate for LACC also suggests room for

improvement. This mortality rate is comparable to that seen in published series on LACC (3.3%–8.9%).^{12–14} However, this is a population-based study of unselected patients, including those treated in emergency surgery and nonexpert centers. The volume–outcome relationship in the present analysis suggests the potential benefit of further specialization and centralization of care in high-volume centers. The small differences in absolute numbers of procedures between low- and high-volume hospitals (2.3 vs 6.9, respectively), as well as the relatively low median volume in the high-volume group (6.9), show that LACC surgery has not yet been centralized in the Netherlands. Further improvement might be expected when annual volumes exceed 15 to 20.¹⁵ The low hospital volumes for LACC-MV might also explain the absence of improvement over time for LACC-MV. Furthermore, lower R0 resection proportions in the emergency and urgent settings suggest a potential role for bridging strategies, such as a decompressing stoma. This would enable optimal staging, potential neoadjuvant treatment, and elective surgery by an optimal surgical team.

A multivisceral resection is essential to achieve an R0 resection in pT4b stage colon cancer and has been associated with improved outcomes at the population level.¹⁶ However, preoperative and intraoperative assessment of organ involvement is often inaccurate because of the difficulty in distinguishing between true tumor invasion and inflammatory adhesions.^{17,18} Reported true pT4 rates

in multivisceral resections were 55%, 36%, and 34% in 3 studies, respectively.^{13,19,20} Therefore, multivisceral resection often turns out to be overtreatment. This is a clinically relevant problem because of the increased morbidity rates, as shown by our results and those of others.^{14,18} Despite its drawbacks, a multivisceral resection seems to be preferred over a less radical approach in clinically adherent tumors with uncertainty regarding the extent of malignant invasion, bearing in mind the negative prognostic impact of an incomplete resection.^{21–23}

In addition to extensive surgery, neoadjuvant therapies could optimize R0 resection proportions in LACC.^{24,25} In contrast to other types of gastrointestinal cancer, administration of neoadjuvant therapy in colon cancer remains uncommon.^{11,14,26,27} Incidental use of a variety of neoadjuvant therapy schedules has been described. In the phase II FOxTROT trial,⁶ 150 patients with LACC were randomized (2:1) between an experimental arm with preoperative chemotherapy (FOLFOX) and a second randomization in RAS wild-type for an anti-EGFR antibody, and a control arm with routine adjuvant chemotherapy only. Preoperative systemic therapy was shown to reduce tumor size and resulted in a significant improvement of R0 resection proportion (96% vs 80%). The need for emergency or urgent surgery, complication rate, and toxicity were comparable across both groups. These findings were confirmed in another phase II study including 22 patients,²⁸ and the PRODIGE 22–ECKINOXE trial with a similar design is currently recruiting.²⁹ In the present study, neoadjuvant therapy was not associated with a higher percentage of R0 resections. This may be the result of both small sample size ($n=77$) and allocation bias, because the most advanced tumors were probably allocated to neoadjuvant therapy.

Because of concerns regarding radiation toxicity, mainly to the small bowel, the use of chemoRT for LACC remains controversial.³⁰ Results of one study in which 33 patients were retrospectively analyzed suggested that neoadjuvant chemoRT combined with en bloc multivisceral resection results in high R0 resection proportions and excellent local control, with acceptable morbidity and mortality.¹⁷ In 64% of these patients, the T4 tumor was located in the sigmoid; it was also the main tumor location (68%) in patients who received neoadjuvant chemoRT in the present study.

Figure 2. Development of the quality of surgical care for LACC.

Abbreviations: LACC, locally advanced colon cancer; MV, multivisceral resection required; noMV, no multivisceral resection required; non-LACC, all other colon cancer resections.

^aPostoperative complicated course: postoperative complication leading to a re-intervention, hospital stay >14 days, or death.

^bR1, incomplete resection with microscopic surgical resection margin involvement; R2, incomplete tumour resection with gross residual tumour that was not resected.

Decisions on neoadjuvant therapy strategies should be based on preoperative imaging, but the accuracy is limited and overstaging rates of up to 50% have been described.^{13,31} In this study, a comparable discrepancy between cT4 and pT4 was found; in 833 of the patients with pT4 tumors, clinical T stage was registered, with 61% being classified as cT1–3. Only 57% of the 578 cT4 tumors were classified as pT4 tumors. Despite its limited accuracy, preoperative imaging seems to be essential when considering neoadjuvant treatment and surgical planning. Therefore, further improvement can be expected from optimal guideline adherence with respect to preoperative imaging and MDT discussion.

LACC is often considered a contraindication for laparoscopic surgery because of oncologic concerns. In this series, laparoscopic surgery was performed in 31% of LACC patients overall and 21% of LACC-MV, with conversion rates of up to 52%. Conversion

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did not lower the R0 resection proportion in patients with LACC-MV, which suggests that it can be considered safe to initiate surgery laparoscopically. In contrast, conversion did result in lower R0 resection proportions in the LACC-noMV group. The latter finding is remarkable and was not confirmed in the literature. Several nonrandomized comparative studies have been published on laparoscopy in LACC.^{11,14,26,27,32,33} The laparoscopic group often had favorable baseline characteristics regarding factors such as previous abdominal surgery and emergency setting. Additionally, resections were less often multivisceral. Conversion rates ranged between 7% and 24%, and R0 resection proportions were mostly similar to those of the open surgery groups. These data are most likely skewed by allocation bias. Increasing the rate of laparoscopic surgery for LACC might contribute to a lower morbidity rate, but this may never jeopardize oncologic safety.

This is a large population-based cohort study, which provides the best available evidence of the nationwide current clinical practice regarding LACC. However, several limitations of this design should be kept in mind. The availability of data is dependent on the self-reported data from the DSCA database, which is subject to registration bias and incomplete data registration. Nonetheless, in order to show accuracy and completeness of data, these were validated on a yearly basis using the Dutch National Cancer Registry.⁷ Furthermore, the variable set is chosen for the purpose of clinical auditing, and several variables relevant to the aim

of this study, such as subdivision in T4a/b subgroups and organ involvement based on pathology reports, are lacking. Additionally, the clinical T stage was unknown in a substantial number of patients, resulting in a small sample size of clinical T4 tumors, which is the relevant group to assess for neoadjuvant strategies. Furthermore, differences in patient and tumor characteristics between subgroups should be recognized when comparing outcome variables between the relevant subgroups.

Conclusions

Among patients who undergo surgery for LACC there is a lower R0 resection proportion and they are at higher risk of postoperative complications and mortality compared with patients who receive surgery for less invasive colon cancer. Neoadjuvant therapy for colon cancer is still rarely applied in the Netherlands and prospective randomized studies must be awaited in order to confirm the observation of more radical resections in phase II studies. Considering the relatively low R0 resection proportion, there is an opportunity for improvement. This may be achieved by optimizing preoperative imaging, the application of neoadjuvant therapy schedules, and centralization and specialization.

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