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Laparoscopic surgery for colon cancer

A systematic review with special focus on real-world data

Worldwide, laparoscopic surgery is becoming the new standard for curative resection of colon cancer. In recent decades, many studies were performed to analyze its advantages and disadvantages and, above all, its oncologic safety compared to the open technique.

Today, there exists quite extensive but also very heterogenous evidence on laparoscopic colorectal tumor surgery. Many publications are dedicated exclusively to postoperative endpoints such as duration of surgery, resection margins, or short-term mortality. Others report long-term outcomes including overall survival or recurrence rates. The study designs range from small case studies to large randomized controlled trials (RCTs), which are regarded as the gold standard in medical research. However, due to strict in- and exclusion criteria, RCTs often reflect the situation in a selected patient collective only; therefore, it might not be sufficient to rely exclusively on the findings of RCTs. In contrast to this, large population-based retrospective multicenter or registry-based studies use “real-world data”, offering insight into the efficiency in daily clinical practice. This renders them an indispensable part of the clinical evaluation process. To account for the lack of randomization, such studies employ adequate statistical methods like

multivariable regression analysis, which needs to be considered when interpreting the corresponding outcomes. This paper is the first systematic review on the topic providing a synthesis of the most important RCTs and relevant retrospective trials, drawing a holistic picture of laparoscopic surgery in colon cancer patients.

Materials and methods

To identify relevant literature on the topic, PubMed and Cochrane Central were searched [1, 2]. For this purpose, three fields of interest were defined:

- *Colorectal cancer*: the corresponding MeSH term is “Colorectal Neoplasms” Moreover, a free-text search with the following (truncated) terms was performed: “colorectal cancer*”, “colorectal carcinoma*”, “colorectal tumor*”, “colorectal tumour*”, and “colorectal neoplasm*”. Local differences in spelling (e.g., “tumour” instead of “tumor”) were considered. To identify only relevant publications, the search was restricted to publications tagged with the subheading “surgery”. Moreover, the free-text search was limited to the title. In total, 91,597 hits were reached.
- *Laparoscopy*: the corresponding MeSH term is “Laparoscopy”. Additionally, a free-text search with the truncated term “laparoscop*”

in all available fields provided by PubMed was performed, leading to identification of 102,255 relevant publications.

- *Open surgery*: the corresponding MeSH term is “Laparotomy”. To also identify relevant literature not tagged by this MeSH term, a free-text search with the truncated terms “laparotomy*”, “celiotomy*”, and “coeliotomy*” in all fields was performed. Thus, 424,689 publications were identified.

In total more than 1800 relevant publications address all three aspects simultaneously, of which more than 1600 were written in English or German (■ Fig. 1). To identify representative high-quality retrospective studies, a selection process based on the widely accepted Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)-criteria [3] was performed. Special focus was placed on the following aspects:

- *Study design*: How was data acquisition performed? How many patients were included? What were the exact in- and exclusion criteria? Is the whole exclusion process transparent for the reader? Is the study collective representative for the population/setting it was gathered from?
- *Study variables*: Is the set of predictor and outcome variables meaningful?

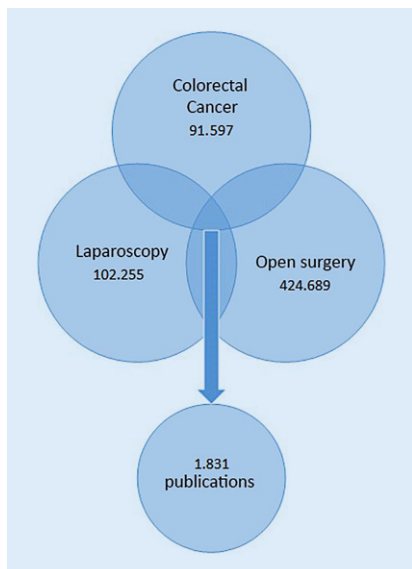


Fig. 1 ▲ Literature research: Number of search hits for publications in PubMed

Are the variable definitions clear and transparent?

- Methods: Were adequate statistical methods applied to account for the lack of randomization? Are all analyses clearly described?

Finally, 14 retrospective studies met the standards for inclusion in the present literature review. A similar workflow was applied to identify 9 relevant RCTs on the topic. **Table 1 and 2** give an overview of the included literature.

Endpoints in the focus of the current review were intraoperative blood loss and duration of surgery, lymphadenectomy and resection margins, postoperative morbidity and mortality, long-term overall survival, and tumor recurrence.

Results

Laparoscopy rate

According to the *Arbeitsgemeinschaft Deutscher Tumorzentren* (ADT; Working Group of German Tumor Centers), the share of laparoscopic resection procedures in Germany has increased from 3.4% in 2000 to 31.0% in 2018 (**Fig. 2**). These figures are based on reports from 30 clinical cancer registries representing approximately one quarter of all colon carcinoma cases in Germany based on

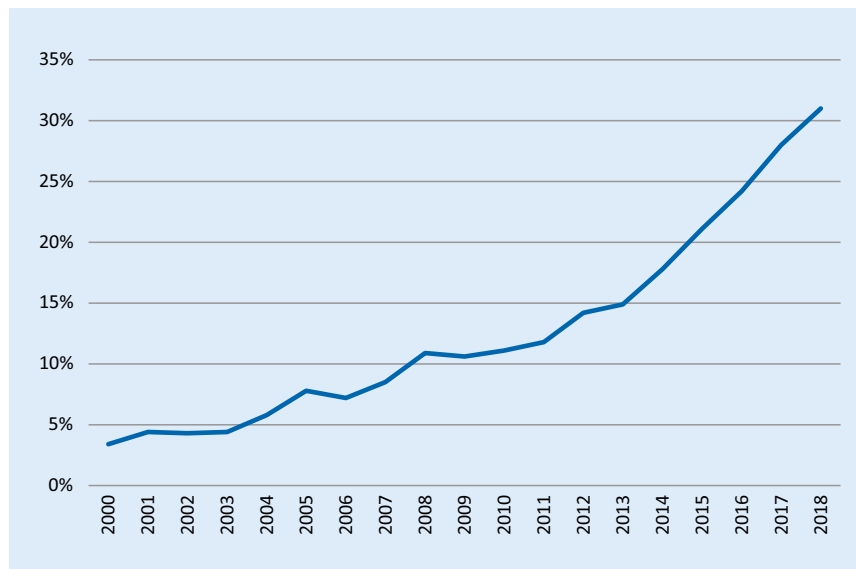


Fig. 2 ▲ Laparoscopy rate in UICC stage I–III colon cancer patients in Germany. Source: *Arbeitsgemeinschaft Deutscher Tumorzentren* (ADT)

data presented at the National Quality Conference of the German Cancer Congress 2020 [4].

Intraoperative blood loss and duration of surgery

In all included RCTs, the mean intraoperative blood loss was significantly lower after laparoscopic surgery. The reported mean values range between 46 and 105 ml compared to 127 to 193 ml after open surgery [5–7]. Similar results can be observed in the population-based trial of McKay et al. from Australia [8], which reports a significantly lower average need for intraoperative blood transfusions of 0.4 vs. 0.7 per patient in favor of the laparoscopic procedure.

Laparoscopic tumor resections take longer than those performed in the conventional technique. The mean duration of surgery in the included RCTs ranged between 142 and 213 min [5–7, 9, 10]. Again, these observations are supported by the findings of McKay et al. [8]. According to their retrospective study, laparoscopic procedures take on average 24 min longer (175 min vs. 151 min; $p < 0.001$).

Lymphadenectomy and resection margins

A sufficient number of removed and histologically evaluated lymph nodes is regarded as a positive quality indicator of successful tumor removal. For example, the German treatment guideline on colorectal carcinoma recommends a minimum count of 12 nodes, although there is no international consensus concerning the exact number [11]. Moreover, there exists no generally recognized standard for the pathological examination of lymph nodes, which has to be considered when comparing and analyzing results of different studies. A systematic review from Kuhry et al. [12] published by the Cochrane Collaboration in 2008 pools the results of five RCTs reporting on lymphadenectomy [5, 7, 13–15]. Compared to the open approach, the number of harvested lymph nodes after laparoscopic procedures is smaller by 1 lymph node (confidence interval, CI: [-1.65–-0.35]). The results of the retrospective trials on this endpoint are comparable (Kofschoten et al. [16]: more than 10 harvested lymph nodes: odds ratio, OR: 0.87, CI: 0.76–1.00, reference: open; McKay et al. [5]: mean count of harvested lymph nodes per patient: laparoscopic intention-to-treat, itt: 17.4 vs. open: 18.2, $p = 0.38$; Völkel et al. [17]:

more than 12 harvested lymph nodes: laparoscopic itt: 88.9% vs. open: 92.2%, $p = 0.028$).

Tumor-free resection margins are the primary goal of each tumor resection. In 2005, the randomized CLASICC trial reported a higher share of tumor-positive margins after laparoscopic procedures [9]. This outcome misses the significance level considerably ($p = 0.45$), but caused an extensive discussion on the topic anyway. Therefore, the real-world data publications are even more interesting. A population-based survey from the US by Zheng et al. [18] observed a significantly lower share of tumor-positive resection margins after laparoscopic procedures (laparoscopic 3.4% vs. open 5.5%; $p < 0.001$), although this advantage is mitigated after risk adjustment and propensity matching. In the study of Kolfshoten et al. [16] the advantage for the laparoscopic procedure remains constant even after risk adjustment (OR: 0.68, CI: 0.48–0.98, reference: open). According to a registry-based trial from southern Germany published in 2018, positive resection margins are less frequently associated with laparoscopic procedures [17]; however, due to a low absolute count of postoperatively tumor-positive patients, significance testing was not possible. Contrary to this, the Australian registry study of McKay et al. [8] reports a (non-significantly) smaller mean distance between tumor border and resection margin in laparoscopic patients.

Postoperative morbidity and mortality

Various trials have shown that laparoscopic patients suffer less from postoperative pain and wound infection, leading to faster convalescence and a shorter hospital stay [16, 19–23]. This was confirmed by a meta-analysis from Schwenk et al. [24] and a systematic review from Otani et al. [25].

There are different outcome measures to quantify postoperative mortality: depending on the trial, in-hospital-, 30-day, or 90-day mortality were evaluated. According to the randomized CLASICC trial, there is no significant difference between laparoscopy and

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Laparoscopic surgery for colon cancer. A systematic review with special focus on real-world data

Abstract

Background. To evaluate a new procedure in daily clinical practice, it might not be sufficient to rely exclusively on the findings of randomized clinical trials (RCTs). This is the first systematic review providing a synthesis of the most important RCTs and relevant retrospective cohort studies on short- and long-term outcomes of laparoscopic surgery in colon cancer patients.

Materials and methods. In a literature search, more than 1800 relevant publications on the topic were identified. Relevant RCTs and representative high-quality retrospective studies were selected based on the widely accepted Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) criteria. Finally, 9 RCTs and 14 retrospective cohort studies were included.

Results. Laparoscopic surgery for colon cancer is associated with a slightly longer duration of surgery, but a variety of studies

show an association with a lower rate of postoperative complications and a shorter duration of hospital stay. Particularly in older patients with more frequent comorbidities, laparoscopy seems to contribute to decreasing postoperative mortality. Concerning long-term oncologic outcomes, the laparoscopic and open techniques were shown to be at least equivalent.

Conclusion. The findings of the existing relevant RCTs on laparoscopic surgery for colon cancer are mostly confirmed by representative retrospective cohort studies based on real-world data; therefore, its further implementation into clinical practice can be recommended.

Keywords

Minimally invasive surgical procedures · Registries · Cohort studies · Randomized controlled trial · Evidence-based medicine

Laparoskopische Chirurgie beim Kolonkarzinom. Eine systematische Übersichtsarbeit mit speziellem Fokus auf „real world data“

Zusammenfassung

Hintergrund. Um die Eignung eines neuen Behandlungsverfahrens im klinischen Alltag zu überprüfen, sollte man sich nicht ausschließlich auf die Ergebnisse randomisierter Studien (RCTs) verlassen. Dies ist die erste Übersichtsarbeit zum Thema laparoskopische Tumorresektion beim Kolonkarzinom, welche neben RCTs repräsentative retrospektive Kohortenstudien zu Kurz- und Langzeitergebnissen berücksichtigt.

Methoden. In einer Literaturrecherche wurden über 1800 relevante Publikationen identifiziert. Eine Selektion der relevanten pro- und retrospektiven Studien zum Thema Laparoskopie beim Kolonkarzinom fand auf Grundlage der STROBE-Kriterien statt. Schließlich wurden 9 RCTs und 14 retrospektive Studien eingeschlossen.

Ergebnisse. Laparoskopische Chirurgie beim Kolonkarzinom ist zwar mit einer etwas längeren Operationsdauer, jedoch auch mit einer niedrigeren postoperativen

Komplikationsrate und einer kürzeren Krankenhausverweildauer assoziiert. Vor allem ältere Patienten mit mehr Komorbiditäten scheinen von einer niedrigeren postoperativen Mortalität zu profitieren. Was das onkologische Langzeitergebnis betrifft, ist das laparoskopische dem offenen Verfahren mindestens ebenbürtig.

Schlussfolgerung. Die Ergebnisse der existierenden relevanten RCTs zur Laparoskopie beim Kolonkarzinom werden größtenteils von repräsentativen retrospektiven Kohortenstudien aus dem Klinikalltag bestätigt. Daher kann die weitere Implementierung der Laparoskopie in den Klinikalltag empfohlen werden.

Schlüsselwörter

Minimal-invasive Chirurgie · Register · Kohortenstudien · Randomisierte kontrollierte Studie · Evidenzbasierte Medizin

Table 1 Randomized clinical trials on laparoscopic and open surgery for colon cancer

	Period of recruitment	Data source	Patients, N	Follow-up
Curet [29]	1993–1995	1 US center	Laparoscopic: 25 Open: 18	59 months
Kaiser [13]	1995–2001	1 US center	Laparoscopic: 28 Open: 28	35 months
Leung [14]	1993–2002	2 Chinese centers	Laparoscopic: 203 Open: 200	51 months
Liang [15]	2000–2004	1 Taiwanese center	Laparoscopic: 135 Open: 134	40 months
Lacy [7]	1993–1998	1 Spanish center	Laparoscopic: 111 Open: 108	95 months
COST [10, 28]	1994–2001	48 US centers	Laparoscopic: 435 Open: 437	84 months
COLOR [6, 30, 31]	1997–2003	29 centers in 8 European countries	Laparoscopic: 627 Open: 621	53 months
CLASICC [9]	1996–2002	27 GB centers	Laparoscopic: 273 Open: 140	56 months
Braga [5]	2000–2004	1 Italian center	Laparoscopic: 134 Open: 134	73 months

Table 2 Representative retrospective cohort studies (RETRO) on laparoscopic and open surgery for colon cancer

	Period of recruitment	Data source	Patients, N	Follow-up
Benz [33]	2003–2011	Germany, ADT dataset using data from 30 regional cancer registries	~37,000 colectomies, laparoscopy rate: 10.7%	Maximum follow-up: 5 years
Bilimoria [34]	1998–2002	USA, National Cancer Database, ~63% of all US cancer diagnoses	231,381, laparoscopy rate: 4.6%	5 years
Fox [23]	2008–2009	USA, Nationwide Inpatient Sample Databases, documenting ~70% of all US cancer diagnoses	~6800 colectomies, laparoscopy rate: 50%	Only short-term
Kolfschoten [16]	2010	Netherlands, Dutch Surgical Colorectal Audit, featuring data from 90 hospitals/93% of all colectomies in the country	~5000 colectomies, laparoscopy rate: 41%	Only short-term
Kube [22]	2000–2003	Germany, <i>Bundesweite Qualitätssicherungsstudie Kolon-/Rektumkarzinome (Primärtumor)</i> database with voluntarily contributed data from 340 hospitals	~13,000 colectomies, laparoscopy rate: 4.4%	Maximum follow-up: 5 Jahre
McKay [8]	2001–2008	6 Australian centers	Laparoscopic: 434, open: 742	Only short-term
Panis [26]	2006–2008	All French cases (registred by programme de médicalisation des systèmes d'information, PMSI)	84,524, laparoscopy rate: 26%	Only short-term
Sammour [21]	2003–2009	3 Australian centers	~58,100 colectomies, laparoscopy rate: 51%	Maximum follow-up: 5 years
Steele [20]	2003–2004	USA, Nationwide Inpatient Sample Databases, documenting ~70% of all US cancer diagnoses	~98,900 colectomies, laparoscopy rate: 3%	Only short-term
Stormark [32]	2007–2010	Norway, National Cancer Registry	~8700 colectomies, laparoscopy rate: 27%	Maximum follow-up: 5 years
Taylor [19]	2006–2008	Great Britain, National Cancer Data Repository, a representative national cancer registry	~58,100 colectomies, laparoscopy rate: 41%	Maximum follow-up: 1 year
Völkel [17, 27, 35]	2004–2013	Representative cancer registry from southern Germany with 1.1 million inhabitants	~2700 colectomies, laparoscopy rate: 16%	Maximum follow-up: 5 years
	2005–2014	Germany, ADT dataset using data from 30 regional cancer registries	~1500 patients aged 80+, laparoscopy rate: 17.1%	Maximum follow-up: 5 years
Zheng [18]	2010–2011	USA, National Cancer Database, documenting ~70% of all US cancer diagnoses	~55,400 colectomies, laparoscopy rate: 41%	Only short-term

Table 3 Postoperative mortality				
	Laparoscopic	Open	Significance	Type of study
In-hospital mortality				
<i>CLASICC</i>	5%	4%	n. s.	RCT
<i>Fox</i>				RETRO
Descriptive	0.7%	1.2%	s	
Risk adjusted	No significant correlation between laparoscopy rate and in-hospital mortality			–
<i>Kube</i>				RETRO
Descriptive	0.7%	2.7%	s.	
<i>McKay</i>				RETRO
Descriptive	0.9%	1.6%	n. s.	
<i>Steele</i>				RETRO
Descriptive	0.6%	1.4%	s.	
30-day postoperative mortality				
<i>Benz</i>				RETRO
Descriptive	3.3%	0.9%	s.	
Risk adjusted	OR left 0.49 OR right 0.6	Reference	left s. right n. s.	
<i>Kolfschoten</i>				RETRO
Descriptive	2.4%	4.9%	–	
Risk adjusted	OR: 0.63	Reference	s.	
<i>Panis</i>				RETRO
Descriptive	2.0%	6.0%	s.	
Risk adjusted	OR: 0.59	Reference	s.	
<i>Sammour</i>				RETRO
Descriptive	0.7%	1.6%	n. s.	
<i>Taylor</i>				RETRO
Risk adjusted	OR: 0.55	Reference	s.	
<i>Zheng</i>				RETRO
Descriptive	1.3%	2.3%	s.	
Risk adjusted	OR: 0.59	Reference	s.	
90-day postoperative mortality				
<i>Völkel</i>				RETRO
Descriptive	2.3%	6.0%	n. s.	
Risk adjusted	OR: 0.53	Reference	n. s.	

s. significant ($p < 0.05$), n. s. not significant, OR odds ratio, RCT randomized controlled trial, RETRO representative retrospective cohort study

laparotomy concerning in-hospital mortality (Table 3), but most registry-based studies show a lower risk of postoperative mortality in laparoscopic patients (OR after multivariable risk adjustment ranges between 0.49 and 0.63, Table 3; [5, 13–20]).

The trials of Panis et al. [26] and Völkel et al. [27] point towards an age- and partial comorbidity-dependent gradient: older patients and patients with a somewhat higher level of comorbidity benefit more from the laparoscopic

approach in terms of postoperative mortality. Based on US registry data, Fox et al. [23] showed a significant association between a higher laparoscopy rate in a hospital and a shorter duration of stay and lower postoperative morbidity. However, postoperative mortality seems to be independent of this. However, it must be acknowledged that in all the studies it was adjusted for many but not all important confounders. Items such as intraabdominal adhesions or lipodisttribution are often poorly documented

and, thus, usually cannot be included in the statistical analyses.

In summary, it seems safe to postulate a positive influence of laparoscopy on postoperative morbidity. An association with lower postoperative mortality is also very likely, particularly in old and comorbid patients. Other aspects of perioperative management including establishment of an ostomy, limited resection, and failure-to-rescue situations supposedly play an even more important role in this context.

Long-term overall survival

“Mortality turned out to be equal in patients who had undergone laparoscopic surgery as compared to patients who underwent open surgery” (OR: 0.82, CI: 0.62–1.09, reference: open). This is the conclusion of the systematic Cochrane review by Kuhry et al. [12], which incorporated four RCTs in the corresponding meta-analysis on long-term survival after laparoscopic and open colon carcinoma resection [7, 13, 28, 29]. Concordantly, the renowned randomized COLOR trial reports almost identical 5-year survival rates after laparoscopic (73.8%; standard deviation, sd: 69.7–77.9%) and open (74.2%, sd: 70.1–78.2%) resection [30]. After a very long observation time of 10 years, the situation has not changed much: “Laparoscopic surgery for non-metastatic colon cancer is associated with similar rates of disease-free survival, overall survival and recurrences as open surgery” [31].

High-quality retrospective studies on long-term survival are scarce. Based on Norwegian cancer registry data, Stormark et al. did not find significant differences between the two surgical techniques concerning overall survival in Union for International Cancer Control (UICC) stage I–III patients (relative survival after 5 years: laparoscopic 77.7% vs. open: 80.6%, $p = 0.54$) [32]. Sammour et al. used Australian registry data and observed superior 5-year survival rates after laparoscopic resection (laparoscopic itt: 75.9% vs. open: 69.2%, $p = 0.015$), although the significance level was no longer reached after risk adjustment [21]. Kube et al. analyzed

Table 4 Long-term survival

	Laparoscopic	Open	Significance	Type of study
Overall mortality risk for the whole long-term observation period				
<i>Benz</i>				
Risk adjusted	HR right 0.67; left 0.7	Reference	Right/left $p < 0,001$	RETRO
<i>Bilimoria</i>				
Risk adjusted				RETRO
UICC I–III	HR 0.91	Reference.	s.	
UICC III	HR 0.97	Reference	n.s.	
<i>Curet</i>	HR: 0.3	Reference	n.s.	RCT
<i>Kaiser</i>	HR: 2.3	Reference	n.s.	RCT
<i>Kuhry (Cochrane review)</i>	HR: 0.84	Reference	n.s.	Meta-analysis
<i>Lacy</i>	HR: 0.6	Reference	n.s.	RCT
5-year overall survival				
<i>Braga</i>	72.0%	64.0%	n.s.	RCT
<i>CLASICC</i>	55.7%	62.7%	n.s.	RCT
<i>COLOR</i>	73.8%	74.2%	n.s.	RCT
<i>COST</i>	76.4%	74.6%	n.s.	RCT
<i>Kube</i>				
Descriptive	82.8% Conversions: 68.7%	66.9%	s	RETRO
<i>Sammour</i>				
Descriptive	75.9%	69.2%	s.	RETRO
Risk adjusted	No significant difference between laparoscopy and laparotomy concerning overall survival			
<i>Völkel</i>				
Overall (perioperative deaths not excluded)	80.2%	69.0%	s.	RETRO
T1–3N0	86.5%	78.8%	s.	
T4/N1–2	72.5%	65.3%	n.s.	
Risk adjusted				
T1–3N0	HR: 0.65	Reference.	s.	
T4/N1–2	HR: 0.98	Reference	n.s.	
Relative 5-year overall survival				
<i>Stormark</i>				
Descriptive	77.7%	80.6%	n.s.	RETRO

s. significant ($p < 0,05$), n.s. not significant, HR hazard ratio, RCT randomized controlled trial, RETRO representative retrospective cohort study, UICC Union for International Cancer Control

data of the An-Institut Magdeburg and also saw a significant advantage for the laparoscopic procedure (5-year overall survival: laparoscopic as treated: 82.8% vs. open: 66.9%, $p = 0.005$), although it must be noted that participation in this retrospective cohort study performed 15 years ago in Germany was voluntary [22].

A more recent study of Benz et al. [33] analyzes cancer registry data from

the *Arbeitsgemeinschaft Deutscher Tumorzentren* (ADT; Working Group of German Tumor Centers), which gathers patient-, diagnosis-, and treatment-related medical records in approximately 30% of German tumor patients on a legal basis. It stratified the patients into four groups: “laparoscopic left”, “laparoscopic right”, “open left”, and “open right”. According to this study, tumor location does not serve as an effect mod-

ifier for the surgical approach. In both the Kaplan–Meier and the multivariable analyses, there was a significant survival benefit for the laparoscopic technique, regardless of tumor location and UICC stage (only stages I–III were included in the analysis).

These findings are in contrast to an earlier analysis of the National Cancer Database (NCDB) registry by Bilimoria et al. [34], who did not observe a positive influence of the laparoscopic approach on overall survival. In the study of Völkel et al., the advantage for the laparoscopic approach was also restricted to low-risk situations (T1–3, N0), while high-risk patients (T4 or N1) did not benefit significantly from the minimally invasive technique [35].

Taking all of the presented evidence (Table 4) into account, the laparoscopic and the open approach seem to be equivalent in terms of overall survival. There might perhaps be a slight advantage for the laparoscopic approach. Future studies on this topic should focus on the standardization of certain surgical standards such as the extent of lymphadenectomy, since this has been neglected by virtually all existing pro- and retrospective trials.

Tumor recurrence

Colorectal tumor resection aims to maximize tumor-free survival. According to the Cochrane meta-analysis by Kuhry et al., laparoscopy and laparotomy do not differ significantly in terms of local and distant metastasis rates [12].

Since local recurrence events are not common in colon cancer patients, most studies simply report disease-free survival. For example, the COLOR study reports a disease-free survival rate of 66.5% (sd 62.2–70.7) in patients with laparoscopic and 67.9% (sd 63.6–72.2) in patients with open resection [30]. Despite the randomized study design, it was decided to additionally perform multivariable Cox regression to adjust for age, sex, and UICC stage, resulting in a hazard ratio (HR) of 0.92 (CI 0.74–1.15, reference: open) in favor of the laparoscopic approach. This figure is almost perfectly matched by the cancer registry study of Völkel et al.: HR 0.94 (CI 0.74–1.19, ref-

Table 5 Tumor recurrence

	Lap	Open	Significance	Type of study
	Local and distant metastasis			
<i>Kuhry (Cochrane review)</i>				Meta-analysis
Locoregional recurrence	OR: 0.84	Reference	n. s.	
Distant recurrence	OR: 0.82	Reference	n. s.	
<i>CLASICC</i>				RCT
Locoregional recurrence	7.3%	5.7%	n. s.	
Distant recurrence	11.4%	12.9%	n. s.	
<i>Kaiser</i>				RCT
Locoregional recurrence	3.6%	0%	n. s.	
Distant recurrence	7.1%	5.0%	n. s.	
<i>Lacy</i>				RCT
Locoregional recurrence	6.6%	13.7%	n. s.	
Distant recurrence	6.6%	8.8%	n. s.	
<i>Liang</i>				RCT
Locoregional recurrence	0%	0%	n. s.	
Distant recurrence	15.6%	19.4%	–	
5-year disease-free survival				
CLASICC	57.6%	64.0%	n. s.	RCT
COLOR	66.5%	67.9%	n. s.	RCT
COST	69.2%	68.4%	n. s.	RCT
5-year recurrence-free survival				
<i>Kube</i>				RETRO
Descriptive	83.2% Conversions: 67.6%	72.5%	s.	
<i>Völkel</i>				RETRO
Descriptive:	75.9%	70.3%	n. s.	
Risk adjusted:	HR: 0.94	Reference	n. s.	

s. significant ($p < 0.05$), n. s. not significant, HR hazard ratio, RCT randomized controlled trial, RETRO representative retrospective cohort study

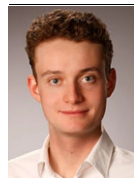
erence: open). However, in the older study by Kube et al., there was no significant difference between the surgical approaches in terms of disease-free survival ([35]; ■ Table 5).

Conclusion

Laparoscopic surgery for colon carcinoma is associated with a slightly longer duration of surgery, but a variety of studies show that it is also associated with a lower rate of postoperative complications and a shorter duration of hospital stay. Particularly in older patients with more comorbidities, laparoscopy seems to contribute to decreasing postoperative mortality. Concerning long-term oncologic outcomes, the laparoscopic and the open techniques were shown

to be at least equivalent with regards to overall and recurrence-free survival. Depending on the characteristics of the observed patient collective, laparoscopy might be slightly superior if the same surgical standards are applied.

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Compliance with ethical guidelines

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This publication does not contain any experiments with patients or animals.

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References

1. National Center for Biotechnology Information (2020) U.S. National library of medicine. <https://www.ncbi.nlm.nih.gov/pubmed/>. Accessed 3 Apr 2020
2. Cochrane Central Register of Controlled Trials (CENTRAL) (2020) Cochrane central register of controlled trials (CENTRAL). <https://www.cochranelibrary.com/central/about-central>. Accessed 3 Apr 2020
3. von Elm E, Altman DG, Egger M et al (2007) The strengthening of reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 370:1453–1457. [https://doi.org/10.1016/S0140-6736\(07\)61602-X](https://doi.org/10.1016/S0140-6736(07)61602-X)
4. Arbeitsgemeinschaft Deutscher Tumorzentren e. V. ADT – für Qualitätssicherung in der Onkologie (2019) Arbeitsgemeinschaft Deutscher Tumorzentren e. V. ADT – für Qualitätssicherung in der Onkologie. <https://www.tumorzentren.de/>. Accessed 12 Feb 2019
5. Braga M, Frasson M, Vignali A et al (2005) Laparoscopic vs. open colectomy in cancer patients: long-term complications, quality of life, and survival. *Dis Colon Rectum* 48:2217–2223. <https://doi.org/10.1007/s10350-005-0185-7>
6. Veldkamp R, Kuhry E, Hop WCJ et al (2005) Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomised trial.

- Lancet Oncol 6:477–484. [https://doi.org/10.1016/S1470-2045\(05\)70221-7](https://doi.org/10.1016/S1470-2045(05)70221-7)
7. Lacy AM, Garcia-Valdecasas JC, Delgado S et al (2002) Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: a randomised trial. *Lancet* 359:2224–2229. [https://doi.org/10.1016/S0140-6736\(02\)09290-5](https://doi.org/10.1016/S0140-6736(02)09290-5)
 8. McKay GD, Morgan MJ, Wong S-KC et al (2012) Improved short-term outcomes of laparoscopic versus open resection for colon and rectal cancer in an area health service: a multicenter study. *Dis Colon Rectum* 55:42–50. <https://doi.org/10.1097/DCR.0b013e318239341f>
 9. Guillou PJ, Quirke P, Thorpe H et al (2005) Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. *Lancet* 365:1718–1726. [https://doi.org/10.1016/S0140-6736\(05\)66545-2](https://doi.org/10.1016/S0140-6736(05)66545-2)
 10. Fleshman JW, Nelson H, Peters WR et al (1996) Early results of laparoscopic surgery for colorectal cancer. Retrospective analysis of 372 patients treated by Clinical Outcomes of Surgical Therapy (COST) Study Group. *Dis Colon Rectum* 39:8
 11. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): S3-Leitlinie Kolorektales Karzinom, Langversion 1.1, 2014, AWMF Registrierungsnummer: 021-0070L, <http://leitlinienprogramm-onkologie.de/Leitlinien.7.0.html> [Stand: 08.2014]
 12. Kuhry E, Schwenk WF, Gaupset R et al (2008) Long-term results of laparoscopic colorectal cancer resection. *Cochrane Database Syst Rev*. <https://doi.org/10.1002/14651858.CD003432.pub2>
 13. Kaiser AM, Kang J-C, Chan LS et al (2004) Laparoscopic-assisted vs. open colectomy for colon cancer: a prospective randomized trial. *J Laparoendosc Adv Surg Tech A* 14:329–334. <https://doi.org/10.1089/lap.2004.14.329>
 14. Leung KL, Kwok SPY, Lam SCW et al (2004) Laparoscopic resection of rectosigmoid carcinoma: prospective randomised trial. *Lancet* 363:1187–1192. [https://doi.org/10.1016/S0140-6736\(04\)15947-3](https://doi.org/10.1016/S0140-6736(04)15947-3)
 15. Liang J-T, Huang K-C, Lai H-S et al. (2007) Oncologic results of laparoscopic versus conventional open surgery for stage II or III left-sided colon cancers: a randomized controlled trial. *Ann Surg Oncol* 14(1):109–117. <https://doi.org/10.1245/s10434-006-9135-4>
 16. Kofschoten NE, van Leersum NJ, Gooiker GA et al (2013) Successful and safe introduction of laparoscopic colorectal cancer surgery in Dutch hospitals. *Ann Surg* 257:916–921. <https://doi.org/10.1097/SLA.0b013e31825d0f37>
 17. Völkel V (2018) Langzeitüberleben nach laparoskopischer und offener Resektion des Kolonkarzinoms – eine bevölkerungsbezogene Analyse. <https://epub.uni-regensburg.de/37757/>. Accessed 17 June 2019
 18. Zheng Z, Jemal A, Lin CC et al (2015) Comparative effectiveness of laparoscopy vs open colectomy among nonmetastatic colon cancer patients: an analysis using the National Cancer Data Base. *J Natl Cancer Inst*. <https://doi.org/10.1093/jnci/dju491>
 19. Taylor EF, Thomas JD, Whitehouse LE et al (2013) Population-based study of laparoscopic colorectal cancer surgery 2006–2008. *Br J Surg* 100:553–560. <https://doi.org/10.1002/bjs.9023>
 20. Steele SR, Brown TA, Rush RM et al (2008) Laparoscopic vs open colectomy for colon cancer: results from a large nationwide population-based analysis. *J Gastrointest Surg* 12:583–591. <https://doi.org/10.1007/s11605-007-0286-9>
 21. Sammour T, Jones IT, Gibbs P et al (2015) Comparing oncological outcomes of laparoscopic versus open surgery for colon cancer: analysis of a large prospective clinical database. *J Surg Oncol* 111:891–898. <https://doi.org/10.1002/jso.23893>
 22. Kube R, Ptok H, Steinert R et al (2008) Clinical value of laparoscopic surgery for colon cancer (Stellenwert der laparoskopischen Chirurgie des Kolonkarzinoms in der klinischen Routine). *Chirurg* 79:1145–1150. <https://doi.org/10.1007/s00104-008-1585-8>
 23. Fox JP, Desai MM, Krumholz HM et al (2012) Hospital-level outcomes associated with laparoscopic colectomy for cancer in the minimally invasive era. *J Gastrointest Surg* 16:2112–2119. <https://doi.org/10.1007/s11605-012-2018-z>
 24. Schwenk W, Neudecker J, Haase O (2015) Evidenzlage der laparoskopischen Chirurgie beim Kolonkarzinom. *Coloproctology* 37:381–390. <https://doi.org/10.1007/s00053-015-0026-7>
 25. Otani T, Otani T, Fisohta N et al (2016) An evidence-based medicine approach to the laparoscopic treatment of colorectal cancer. *Fukushima J Med Sci*. <https://doi.org/10.5387/fms.2016-4>
 26. Panis Y, Maggiori L, Caranhac G et al (2011) Mortality after colorectal cancer surgery: a French survey of more than 84,000 patients. *Ann Surg* 254:738. <https://doi.org/10.1097/SLA.0b013e31823604ac>
 27. Völkel V, Draeger T, Schnitzbauer V et al (2019) Surgical treatment of rectal cancer patients aged 80 years and older—a German nationwide analysis comparing short- and long-term survival after laparoscopic and open tumor resection. *Eur J Surg Oncol*. <https://doi.org/10.1016/j.ejso.2019.05.005>
 28. (2004) Laparoscopically assisted colectomy is as safe and effective as open colectomy in people with colon cancer Abstracted from: Nelson H, Sargent D, Wieand HS, et al; for the Clinical Outcomes of Surgical Therapy Study Group. A comparison of laparoscopically assisted and open colectomy for colon cancer. *N Engl J Med* 2004; 350: 2050–2059. *Cancer Treat Rev* 30: 707–709. <https://doi.org/10.1016/j.ctrv.2004.09.001>
 29. Curet MJ, Putrakul K, Pitcher DE et al (2000) Laparoscopically assisted colon resection for colon carcinoma: perioperative results and long-term outcome. *Surg Endosc* 14:1062–1066
 30. Buunen M, Veldkamp R, Hop WCJ et al (2009) Survival after laparoscopic surgery versus open surgery for colon cancer: long-term outcome of a randomised clinical trial. *Lancet Oncol* 10:44–52. [https://doi.org/10.1016/S1470-2045\(08\)70310-3](https://doi.org/10.1016/S1470-2045(08)70310-3)
 31. FDeijen CL, Deijen CL, FVasmel JE et al (2016) Ten-year outcomes of a randomised trial of laparoscopic versus open surgery for colon cancer. *Surg Endosc*. <https://doi.org/10.1007/s00464-016-5270-6>
 32. Stormark K, Stormark K, FSoreide K et al (2016) Nationwide implementation of laparoscopic surgery for colon cancer: short-term outcomes and long-term survival in a population-based cohort. *Surg Endosc*. <https://doi.org/10.1007/s00464-016-4819-8>
 33. Benz S, Barlag H, Gerken Met al (2016) Laparoscopic surgery in patients with colon cancer: a population-based analysis. *Surg Endosc*. <https://doi.org/10.1007/s00464-016-5266-2>
 34. Bilimoria KY, Bentrem DJ, Nelson H et al (2008) Use and outcomes of laparoscopic-assisted colectomy for cancer in the United States. *Arch Surg* 143:832. <https://doi.org/10.1001/archsurg.143.9.832>
 35. Völkel V, Draeger T, Gerken Met al (2018) Long-term oncologic outcomes after laparoscopic vs. open colon cancer resection: a high-quality population-based analysis in a southern German district. *Surg Endosc*. <https://doi.org/10.1007/s00464-018-6158-4>