



# Disease-free survival after complete mesocolic excision compared with conventional colon cancer surgery: a retrospective, population-based study

Claus Anders Bertelsen, Anders Ulrich Neuwenschwander, Jens Erik Jansen, Michael Wilhelmsen, Anders Kirkegaard-Klitbo, Jutaka Reilin Tenma, Birgitte Bols, Peter Ingeholm, Leif Ahrenst Rasmussen, Lars Vedel Jepsen, Else Refsgaard Iversen, Bent Kristensen, Ismail Gögenur, on the behalf of the Danish Colorectal Cancer Group

## Summary

**Background** Application of the principles of total mesorectal excision to colon cancer by undertaking complete mesocolic excision (CME) has been proposed to improve oncological outcomes. We aimed to investigate whether implementation of CME improved disease-free survival compared with conventional colon resection.

**Methods** Data for all patients who underwent elective resection for Union for International Cancer Control (UICC) stage I–III colon adenocarcinomas in the Capital Region of Denmark between June 1, 2008, and Dec 31, 2011, were retrieved for this population-based study. The CME group consisted of patients who underwent CME surgery in a centre validated to perform such surgery; the control group consisted of patients undergoing conventional colon resection in three other hospitals. Data were collected from the Danish Colorectal Cancer Group (DCCG) database and medical charts. Patients were excluded if they had stage IV disease, metachronous colorectal cancer, rectal cancer ( $\leq 15$  cm from anal verge) in the absence of synchronous colon adenocarcinoma, tumour of the appendix, or R2 resections. Survival data were collected on Nov 13, 2014, from the DCCG database, which is continuously updated by the National Central Office of Civil Registration.

**Findings** The CME group consisted of 364 patients and the non-CME group consisted of 1031 patients. For all patients, 4-year disease-free survival was 85.8% (95% CI 81.4–90.1) after CME and 75.9% (72.2–79.7) after non-CME surgery (log-rank  $p=0.0010$ ). 4-year disease-free survival for patients with UICC stage I disease in the CME group was 100% compared with 89.8% (83.1–96.6) in the non-CME group (log-rank  $p=0.046$ ). For patients with UICC stage II disease, 4-year disease-free survival was 91.9% (95% CI 87.2–96.6) in the CME group compared with 77.9% (71.6–84.1) in the non-CME group (log-rank  $p=0.0033$ ), and for patients with UICC stage III disease, it was 73.5% (63.6–83.5) in the CME group compared with 67.5% (61.8–73.2) in the non-CME group (log-rank  $p=0.13$ ). Multivariable Cox regression showed that CME surgery was a significant, independent predictive factor for higher disease-free survival for all patients (hazard ratio 0.59, 95% CI 0.42–0.83), and also for patients with UICC stage II (0.44, 0.23–0.86) and stage III disease (0.64, 0.42–1.00). After propensity score matching, disease-free survival was significantly higher after CME, irrespective of UICC stage, with 4-year disease-free survival of 85.8% (95% CI 81.4–90.1) after CME and 73.4% (66.2–80.6) after non-CME (log-rank  $p=0.0014$ ).

**Interpretation** Our data indicate that CME surgery is associated with better disease-free survival than is conventional colon cancer resection for patients with stage I–III colon adenocarcinoma. Implementation of CME surgery might improve outcomes for patients with colon cancer.

**Funding** Tvergaards Fund and Edgar and Hustru Gilberte Schnohrs Fund.

## Introduction

Improvements in the treatment of patients with rectal cancer in the past three decades have resulted in higher survival than patients undergoing treatment for colon cancer.<sup>1</sup> A major factor has been the implementation of total mesorectal excision.<sup>2</sup> A similar change of surgical technique has not been implemented in colon cancer surgery, although it has been suggested that the principles of total mesorectal excision could also be applied in colon cancer surgery through complete mesocolic excision (CME).<sup>3,4</sup> In CME, dissection is done in the embryologically defined mesocolic planes to create an intact envelope of the mesocolic fascia, and all

lymph nodes along the tumour supplying vessels are contained in the specimen.<sup>4</sup> The specimens are characterised by a greater distance from the tumour to the ligation of the tumour supplying vessels. The technique remains controversial,<sup>5,6</sup> and the evidence of increased disease-free survival after CME is mainly based on two single centre studies by Hohenberger and colleagues<sup>4</sup> and Bokey and colleagues.<sup>7</sup> The improvements suggested in these studies could be confounded because historical control groups were used. Because it seems impossible to conduct randomised controlled trials of this technique,<sup>6</sup> population studies comparing CME with conventional

*Lancet Oncol* 2015; 16: 161–68

Published Online  
December 31, 2014  
[http://dx.doi.org/10.1016/S1470-2045\(14\)71168-4](http://dx.doi.org/10.1016/S1470-2045(14)71168-4)

See [Comment](#) page 121

Department of Surgery (C A Bertelsen MD, A U Neuwenschwander MD, J E Jansen MD, L A Rasmussen MD, L V Jepsen MD, E R Iversen MD) and Department of Clinical Physiology (B Kristensen MD), Hillerød University Hospital, Hillerød, University of Copenhagen, Copenhagen, Denmark; Department of Surgical Gastroenterology, Hvidovre University Hospital, Hvidovre, University of Copenhagen, Copenhagen, Denmark (M Wilhelmsen MD); Department of Surgery (A Kirkegaard-Klitbo MD) and Department of Pathology (B Bols MD, P Ingeholm MD), Herlev University Hospital, University of Copenhagen, Copenhagen, Denmark; Department of Surgery, Bispebjerg University Hospital, København NV, University of Copenhagen, Copenhagen, Denmark (J R Tenma MD); and Department of Surgery, Køge Roskilde University Hospital, Køge, University of Copenhagen, Copenhagen, Denmark (Prof I Gögenur)

Correspondence to:  
Dr Claus Anders Bertelsen, Department of Surgery, Hillerød University Hospital, Dyrehavevej 29, DK-3400 Hillerød, Denmark  
[cabertelsen@gmail.com](mailto:cabertelsen@gmail.com)

colon cancer resections might be the only way to clarify any differences between conventional resections and CME.

In June, 2008, CME was implemented for colon cancer at Hillerød Hospital, Denmark, because we were convinced that it would improve oncological outcomes.<sup>8</sup> After a short implementation period, with a few non-CMEs performed, CME has been undertaken as the standard procedure for all elective cases in Hillerød. The

three other centres in the Capital Region of Denmark have been reluctant to implement CME during the study period.<sup>5</sup> These four centres cover the entire population of 1·75 million inhabitants of the Capital Region of Denmark.

During 2009, multidisciplinary team courses were held in Denmark to improve the outcome for colorectal cancer. As part of these courses, the quality of the colon cancer resection specimens of the participating departments was evaluated by external expert pathologists.<sup>9</sup> They showed substantial differences between specimens from Hillerød and those from the other three centres. The CME specimens from Hillerød had a significantly greater lymph node yield, greater distance between the tumour and vascular high tie, and more intact mesocolic fascia.

The aim of this study was to investigate whether implementation of CME surgery was associated with improved disease-free survival compared with conventional colon cancer surgery.

## Methods

### Study design and participants

Data for all patients who underwent elective resection for Union for International Cancer Control (UICC) stage I–III colon adenocarcinomas in the Capital Region of Denmark between June 1, 2008, and Dec 31, 2011, were retrieved from the national database of the Danish Colorectal Cancer Group (DCCG). The CME group consisted of patients who underwent CME in Hillerød; the control group consisted of patients who underwent elective conventional colon resection for adenocarcinomas at one of the three other colorectal cancer centres. None of these three cancer centres performed CME in the study period. All four hospitals are public university hospitals associated with Copenhagen University with patient referral based on postal address.

Medical records of all the patients were reviewed by a colorectal surgeon from Hillerød, and DCCG data were supplemented with data for follow-up. Data from pathological examination of the specimens were retrieved from the DCCG database and missing data were retrieved from pathology reports by colorectal pathologists. Patients were excluded if they had stage IV disease, metachronous colorectal cancer, rectal cancer ( $\leq 15$  cm from anal verge) in the absence of synchronous colon adenocarcinoma, tumour of the appendix, or R2 resections. Survival data were collected on Nov 13, 2014, from the DCCG database, which is continuously updated by the National Central Office of Civil Registration.

To ensure the validity of the data, all patient data in the CME group were audited by the three coauthors (MW, AK-K, and JRT) presenting each of the three centres contributing non-CME patients. Data in the non-CME group were first audited by the primary author for discrepancies between data from the review of medical records by a Hillerød surgeon and those in the DCCG database. Subsequently, all patients in the non-CME group with events in favour of better outcome after CME

	Non-CME (n=1031)	CME (n=364)	p value
Age (years)	73·0 (66·0–79·9)	71·5 (64·3–77·8)	0·021*
Men	472 (46%)	188 (52%)	0·054†
BMI (kg/m <sup>2</sup> )	24·8 (22·5–27·8)	25·0 (22·3–28·4)	0·43*
ASA score			0·0024†
ASA score I	226 (22%)	98 (27%)	..
ASA score II	660 (64%)	196 (54%)	..
ASA score III–IV	145 (14%)	70 (19%)	..
Tumour site of primary tumour			0·59†
Caecum	227 (22%)	79 (22%)	..
Ascending colon	138 (13%)	50 (14%)	..
Hepatic flexure	64 (6%)	16 (4%)	..
Transverse colon	100 (10%)	46 (13%)	..
Splenic flexure	35 (3%)	10 (3%)	..
Descending colon	40 (4%)	17 (5%)	..
Sigmoid colon	427 (41%)	146 (40%)	..
Synchronous tumours	35 (3%)	13 (4%)	..
Tumour site (side)‡			0·50†
Left sided tumour(s)	531 (52%)	175 (48%)	..
Right sided tumour(s)	479 (47%)	182 (50%)	..
Both sides	18 (2%)	7 (2%)	..
Primary colon resection			<0·0001†
Right hemicolectomy	415 (40%)	104 (29%)	..
Extended right hemicolectomy	35 (3%)	65 (18%)	..
Transverse colectomy	17 (2%)	0	..
Right sided subtotal colectomy	18 (2%)	19 (5%)	..
Left hemicolectomy	110 (11%)	35 (10%)	..
Sigmoid resection	403 (39%)	132 (36%)	..
Other segmental resection	1 (<1%)	0	..
Colectomy	29 (3%)	7 (2%)	..
Proctocolectomy	3 (<1%)	2 (<1%)	..
Supplementary colon resection	11 (1%)	4 (1%)	0·96†
Laparoscopic	667 (65%)	179 (49%)	<0·0001†
Conversion to open surgery	129/796 (16%)	52/231 (22%)	0·059†
Resection of other organ	146 (14%)	39 (11%)	0·096†
Fixation of tumour	177 (17%)	46 (12%)	0·043†
30-day mortality	38 (4%)	17 (5%)	0·41†

Data are median (IQR) or n (%). CME=complete mesocolic excision. ASA=American Society of Anesthesiologists. Tumour site of primary tumour=colon tumour with highest T and subsequent N stage in case of synchronous adenocarcinomas. Tumour site (side)=missing data for location of transverse colon cancers in three patients in the non-CME group. Supplementary colon resection=resection of two separate segments—eg, invasion of sigmoid tumour in the caecum → sigmoid resection and supplementary—eg, ileocaecal resection. Laparoscopic=completed laparoscopically. Conversion to open surgery=conversion of intended laparoscopic resection. Resection of other organ did not include other segment of the colon or rectum. Fixation of tumour was assessed by surgeon not by pathologist \*t test. †Pearson's  $\chi^2$  test. ‡n=1028 in the non-CME group.

**Table 1: Baseline and tumour characteristics, surgical procedures done, and 30-day mortality**

Download English Version:

<https://daneshyari.com/en/article/3993518>

Download Persian Version:

<https://daneshyari.com/article/3993518>

[Daneshyari.com](https://daneshyari.com)