## Total mesocolic excision for colon cancer

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## Introduction

- Over the past 2 decades the role of TME in the management of rectal cancer has been well established.
  - Involves sharp pelvic dissection & preservation of the fascia propria of the rectum
  - The rectum, its blood supply and draining lymph nodes are contained within this tissue envelope
  - This is associated with decreased local recurrence and improved patient outcomes

## Introduction

- Are similar surgical principles are important in the management of colon cancer?
- Concept of complete mesocolic excision (CME)

Pathology grading of colon cancer surgical resection and its association with survival: a retrospective observational study

Nicholas P West, Eva J A Morris, Olorunda Rotimi, Alison Caims, Paul J Finan, Philip Quirke

- Hypothesized that removal of an intact mesocolon may be associated with improved outcomes after resection of colon cancer
- Retrospective review of all colon cancer resections at Leeds General Infirmary between 1997 and 2002
- Standard practice to photograph all fixed surgical specimens before serial slicing

 The quality of the mesocolic specimen was graded based on a system developed for the MRC Classic trial

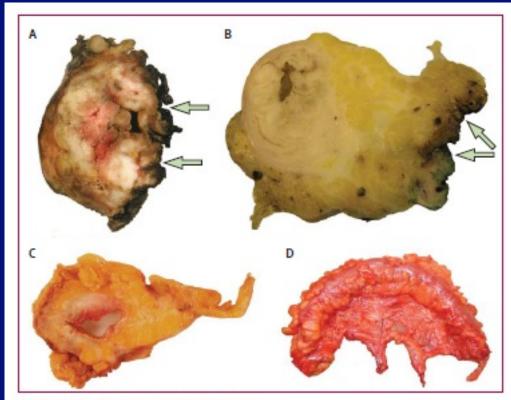


Figure 1: Grading of the plane of mesocolic dissection

(A) Muscularis propria plane (arrows show areas of exposed muscularis propria). (B) Intramesocolic plane (arrows show disruption of the mesocolon but the incisions do not reach down to the muscularis propria). (C) Mesocolic plane (smooth intact mesocolic excision). (D) Mesocolic plane with high vascular ties close to the aorta (courtesy of Prof P-O Nystrom, Stockholm, Sweden).

- 521 resections performed
  - 122 lacked adequate photographs
- 399 specimens were included
  - 338 patients treated with curative intent
  - 61 treated with palliative intent
  - No patients were treated with high vascular ligation

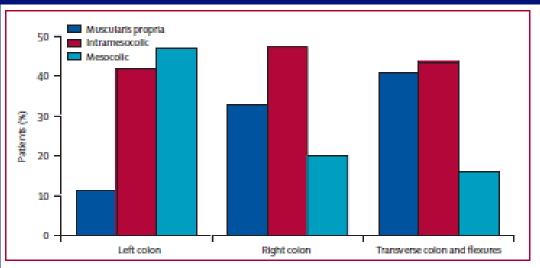


Figure 3: Percentage of excisions resected in the muscularis propria, intramesocolic, or mesocolic planes, according to the site of the primary tumour

Inter-observer Agreement 85%

- The quality of surgery was higher for patients treated with curative intent
- The median lymph node harvest was 14.5
  - This did not differ according to the plane of surgery
- Cross sectional tissue area was greater for mesocolic plane surgery compared to muscualris propria plane and intra-mesocolic plane surgery

## Results: all patients

	All patients (n=399)		Curative excisions (n=338)		
	HR (95% CI)	P	HR (95% CI)	P	
Age (per 10-year increase)	1-43 (1-23-1-67)	<0.0001	1-52 (1-26-1-83)	<0.0001	
Surgery type					
Curative	1-00	_	_	_	
Palliative	3-56 (2-39-5-30)	<0.0001	_		
T-stage					
3	1-00	_	1.00		
1 and 2	1-14 (0-57-2-30)	0.713	1.00 (0.49-2.04)	0-997	
4	1-94 (0-93-4-02)	0-077	1-90 (0-90-4-02)	0-091	
N-stage					
0	1-00	_	1.00		
1	1-31 (0-90-1-93)	0.163	1-16 (0-74-1-81)	0-511	
2	2-25 (1-49-3-40)	<0.0001	2-95 (1-78-4-56)	<0.0001	
Plane of surgery					
Muscularis propria	1.00	_	1.00		
Intramesocolic	0-81 (0-56-1-16)	0.244	0-69 (0-43-1-10)	0.117	
Mesocolic	0-86 (0-56-1-31)	0.472	0.70 (0.43-1.14)	0.153	
HR-haz ard ratio. CT-chemothe	гару.				

Factors associated with overall survival

## Results: patients with stage III disease

	All patients (n=16	i1)	Curative excisions (n=154)			
	HR (95% CI)	P	HR (95% CI)	P		
Age (per 10-year increase)	1.26 (0.97-1.65)	0.082	1-26 (0-95-1-66)	0.111		
Surgery type						
Curative	1-00	_	_	_		
Palliative	4-22 (1-80-9-89)	<0.0001	-	_		
T-stage						
3	1-00	_	1-00	_		
1 and 2	0-48 (0-06-3-62)	0-477	0-49 (0-65-3-68)	0.487		
4	2.20 (1.35-3.58)	<0.0001	2-20 (1-34-3-60)	<0.0001		
N-stage						
1	1-00	_	1-00	_		
2	2.19 (1.37-3.50)	<0.0001	2-38 (1-46-3-88)	<0.0001		
Post-operative CT						
No	1-00	_	1.00	_		
Yes	0-44 (0-25-0-78)	0.005	0.44 (0.24-0.79)	0.006		
Plane of surgery						
Muscularis propria	1-00	-	1-00	_		
Intramesocolic	0-48 (0-27-0-86)	0.013	0-55 (0-30-1-02)	0.059		
Mesocolic	0-45 (0-24-0-85)	0-014	0.50 (0.26-0.98)	0.043		
HR-hazard ratio. CT-chemotherapy.						

Factors associated with overall survival

#### Conclusions

- Authors suggest that high quality colon cancer surgery involves dissection in the mesocolic plane
  - Produces an intact peritoneal-lined mesentary and a smooth fasciallined surface that contains the primary tumor, its blood supply and lymphatics
  - Surgical disruption of this plane risks tumor spillage
- This is associated with a survival benefit in patients with stage III disease
- The optimal extent of mesenteric resection remains unclear
  - Conflicting results associated with radical excision may reflect nonstandardized surgical technique (non CME surgery)

# Standardized surgery for colonic cancer: complete mesocolic excision and central ligation – technical notes and outcome

W. Hohenberger\*, K. Weber\*, K. Matzel\*, T. Papadopoulos† and S. Merkel\*

\*Department of Surgery, University Hospital, Erlangen, Germany and †Department of Pathology, Vivantes Humboldt Hospital, Berlin, Germany

- Describe their series of 1438 patients who underwent R0 resections for colon cancer at a single institution from 1978-2002
- Compared outcomes for 3 time frames
  - **1978-1984**
  - 1985-1994
  - **1995-2002**

#### Methods

- Right hemicolectomy involved
  - Kocherization of the duodenum division of vessels on the SMV and SMA

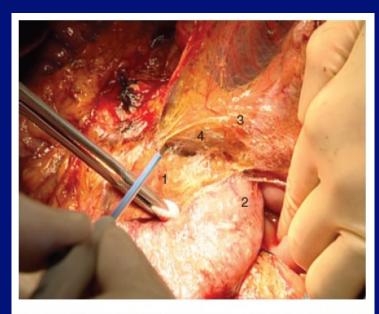


Figure 2 The uncinate process with the mesopancreas (1) and the inferior part of the duodenum (2) is separated from the mesenteric root (3) covered by the right mesocolon ensuring full access to the root of the superior mesenteric vein which is still covered by the mesocolon (4), again with strict preservation of the covering visceral planes (mesopancreas, mesocolon).



#### Methods

- Resection of left sided tumors involved
  - Mobilization of the splenic flexure
  - Division of the IMV at the inferior border of the pancreas
  - Division of the IMA on the aorta

<b>Table I</b> Patient and tumor characteristics ( $n = 1438$ ).				
	n (%)			
Sex				
Male	800 (55.6)			
Female	638 (44.4)			
Age median/range (years)	65 /24–93			
Tumor site				
Cecum	118 (8.2%)			
Appendix	2 (0.1%)			
Ascending colon	211 (14.7%)			
Hepatic flexure	73 (5.1%)			
Transverse colon	129 (9.0%)			
Splenic flexure	63 (4.4%)			
Descending colon	81 (5.6%)			
Sigmoid colon	761 (52.9%)			
Emergency presentation				
No	1302 (90.5%)			
Yes	136 (9.5%)			
Extended resection	271 (18.8%)			
Multivisceral resection	179 (12.4%)			
Adjuvant radiochemotherapy	11 (0.8%)			
Adjuvant chemotherapy	81 (5.6%)			

Table 2 Postoperative complications.

	n	%
Patients with complications	283	19.7
Surgical complications		
Anastomotic leak	38	2.6
Peritonitis	10	0.7
Bleeding	13	0.9
Fistula	6	0.4
Abscesses	20	1.4
Sepsis	10	0.7
Ileus	11	0.8
Wound infection	49	3.4
Urologic	43	3.0
Nonsurgical complications		
Pulmonary	63	4.4
Cardiologic	19	1.3
Neurologic	12	0.8
Nephrologic	19	1.3
Others	37	2.6
Postoperative deaths	45	3.1

- Median lymph node harvest 32 nodes (2-169)
- Recurrence

**Table 3** Locoregional recurrence M0 R0 1978–2002 (5-year rates, n = 1329).

	n	5-Y-LR	95% CI
A 11	1220	4.0	27.61
All	1329	4.9	3.7–6.1
pT1	118	0.9	0-2.7
pT2	186	1.2	0-2.8
pT3	851	5.2	3.6-6.8
pT4	174	10.7	5.8-15.6
pN0	831	1.5	0.7-2.3
pN1	319	6.5	3.6-9.4
pN2	179	20.7	13.8-27.6
Stage I	251	0.4	0-1.2
Stage II	580	2.0	0.8-3.2
Stage III	498	11.1	8.2-14.0
1978–1984	411	6.5	4.0-9.0
1985–1994	514	4.6	2.6-6.6
1995–2002	404	3.6	1.6-5.6

Provide no data on distant mets

## 5-year cancer related survival

#### Multivariate analysis

Stage I	251	99.1	97.7–100	< 0.001			
				< 0.001			
Stage II	580	91.4	89.0–93.8				
Stage III	498	70.2	66.1–74.3				
Low grade	1079	87.9	85.9–89.9	< 0.001	1.0		
High grade	249	72.0	66.1–77.9		1.1	0.8-1.6	0.398
Grade unknown	1						
EVI –	1092	89.6	87.6-91.6	< 0.001	1.0		
EVI +	177	61.9	54.5-69.3		1.7	1.2-2.3	0.003
EVI unknown	60						
No Intraoperative TCD	1300	85.2	83.2-87.2	0.057			
Intraoperative TCD	29	75.0	58.9-91.1				
≥ 28 rln examined	824	86.1	83.7-88.5		1.0		
< 28 rln examined	505	83.1	79.8-86.4	0.144	1.9	1.4-2.5	< 0.001
Elective surgery	1219	86.8	84.8-88.8	< 0.001	1.0		
Emergency presentation	110	83.6	74.0-93.2		1.9	1.3-2.7	< 0.001
1995-2002	404	89.1	86.0-92.2		1.0		
1985-1994	514	84.1	80.8-87.4		1.2	0.8-1.8	0.414
1978–1984	411	82.1	78.4–85.8	0.039	1.2	0.8-1.7	0.285

Stage I	251	99.1	97.7-100
Stage II	580	91.4	89.0-93.8
Stage III	498	70.2	66.1-74.3

Stage	5-year relative survival
T	93%
IIA	85%
IIB	72%
IIIA	83%
IIIB	64%
IIIC	44%
IV	8%

#### Conclusions

- Data suggest that there may be a survival benefit associated with this CME & CVL
  - Very few patients received adjuvant chemotherapy

- Difficult to generalize based on a single institution study
- There are no data that prospectively compare CME/CVL approach with traditional excision

## Complete Mesocolic Excision With Central Vascular Ligation Produces an Oncologically Superior Specimen Compared With Standard Surgery for Carcinoma of the Colon

Nicholas P. West, Werner Hohenberger, Klaus Weber, Aristoteles Perrakis, Paul J. Finan, and Philip Quirke

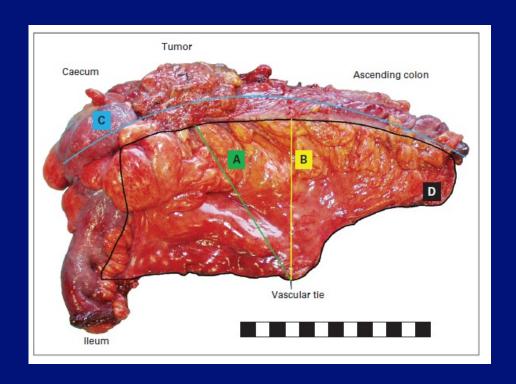
 Sought to examine the potential benefit of central vascular ligation at the time of complete mesocolic excision (CME) in patients with colon cancer

#### Methods

- Included patients treated at 2 institutions
  - 49 from Erlangen, Germany prospectively enrolled from 2007-2008
  - Open resections by 9 surgeons
  - CME with CVL is the established approach
  - 40 patients from Leeds, England, 25 prospectively enrolled in 2008 and
     15 retrospectively identified from 1999-2003
  - Open and laparoscopic cases by 10 surgeons
  - CME and CVL not practiced

#### Methods

- Specimen photographs were examined
- Outcomes were compared
  - Grade of surgical plane
  - Tissue morphometry
  - Lymph node harvest



- Demographic and tumor factors were similar among patients from the two hospitals except:
  - German cohort tumors more likely to be poorly differentiated
  - Leeds cohort included more right hemicolectomy specimens

## Results: lymph nodes

Parameter	Erlangen	Leeds	P
Median No. of lymph nodes retrieved	30	18	< .0001
IQR	23-39	12-24	
Positive nodes retrieved			
All patients			
Median	0	1	.241
IQR	0-2	0-3	
N1/2 patients			
Median	4	3	.923
IQR	1-6	1-6	
Negative nodes retrieved			
All patients			
Median	28	16	< .0001
IQR	21-38	10-22	
N1/2 patients			
Median	26	12	< .0001
IQR	18-33	5-17	
Lymph node ratio			
All patients			
Median	0	3	.110
IQR	0-6	0-29	
N1/2 patients			
Median	10	27	.019
IQR	4-24	8-53	

NOTE. Positive nodes are those containing histologic evidence of metastatic carcinoma. Negative nodes show no evidence of metastatic spread. Lymph node ratio is the percentage of lymph nodes retrieved that contain metastatic carcinoma. Abbreviation: IQR, interquartile range.

## Results: grade of surgery

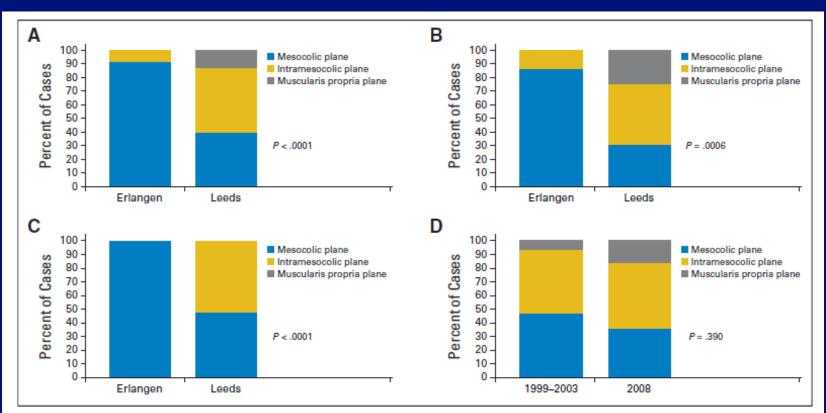


Fig 2. Percentage distribution of the plane of surgery (mesocolic, intramesocolic, or muscularis propria) according to institution or time period for (A) all patients, (B) right-sided resections, (C) left-sided resections, and (D) Leeds patients collected retrospectively (1999-2003) and prospectively (2008).

## Results: tissue morphometry

Table 3. Median Tissue Morphometry Measurements for Patients From Erlangen and Leeds According to Side of Resection (right or left)

Resection by Side	Erlangen	Leeds	P
Right			
Tumor to HVT, mm	128.7	81.4	< .0001
Normal bowel to HVT, mm	101.6	72.4	.007
Length of large bowel, mm	264.9	183.2	.002
Length of small bowel, mm	83.3	60.3	.003
Area of mesentery, mm <sup>2</sup>	16,769.6	8,881.0	< .0001
Left			
Tumor to HVT, mm	145.0	97.0	.001
Normal bowel to HVT, mm	107.6	85.1	.044
Length of large bowel, mm	392.2	260.3	< .0001
Area of mesentery, mm <sup>2</sup>	24,127.5	13,166.2	< .0001

Abbreviation: HVT, high vascular ties.

### Conclusions

- CME and CVL is associated with excision of more mesentary compared to standard excisions
- This may explain the proposed survival benefit associated with this surgical technique

#### What do these studies mean?

- CME and CVL are separate concepts
- There it not enough evidence to support incorporation of CME with CVL into routine practice
  - What are the risks?
- CME alone deserves consideration
  - Likely can be easily performed and taught to residents
  - Little risk and may be potential benefit
- Further research is needed to define the role of these surgical approaches

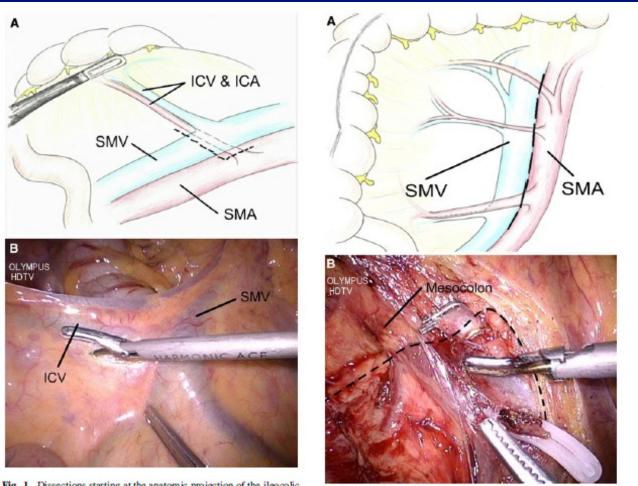


Fig. 1 Dissections starting at the anatomic projection of the ileocolic vessel (A diagram, B photo)

Fig. 2 The dissection proceeds along the SMV to excise out the vessels (A diagram, B photo)

CME, CVL and laparoscopic colectomy