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Colonic stenting versus emergency surgery for acute left-sided malignant colonic obstruction: a multicentre randomised trial

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Summary

Background Colonic stenting as a bridge to elective surgery is an alternative for emergency surgery in patients with acute malignant colonic obstruction, but its benefits are uncertain. We aimed to establish whether colonic stenting has better health outcomes than does emergency surgery.

Methods Patients with acute obstructive left-sided colorectal cancer were enrolled from 25 hospitals in the Netherlands and randomly assigned (1:1 ratio) to receive colonic stenting as a bridge to elective surgery or emergency surgery. The randomisation sequence was computer generated with permuted blocks and was stratified by centre; treatment allocation was concealed by use of a web-based application. Investigators and patients were unmasked to treatment assignment. The primary outcome was mean global health status during a 6-month follow-up, which was assessed with the QL2 subscale of the European Organisation for Research and Treatment of Cancer quality-of-life questionnaire (EORTC QLQ-C30). Analysis was by intention to treat. This study is registered, number ISRCTN46462267.

Findings Between March 9, 2007, and Aug 27, 2009, 98 patients were assigned to receive colonic stenting (n=47 patients) or emergency surgery (n=51). Two successive interim analyses showed increased 30-day morbidity in the colonic stenting group, with an absolute risk increase of 0·19 (95% CI –0·06 to 0·41) in analysis of the first 60 patients (14 of 28 patients receiving colonic stenting *vs* 10 of 32 receiving emergency surgery), and an absolute risk increase of 0·19 (–0·01 to 0·37) in analysis of the first 90 patients (23 of 47 patients *vs* 13 of 43). In accordance with the advice of the data safety monitoring committee, the study was suspended on Sept 18, 2009, and ended on March 12, 2010. At the final analysis of 98 patients, mean global health status during follow-up was 63·0 (SD 23·8) in the colonic stenting group and 61·4 (SD 21·9) in the emergency surgery group; after adjustment for baseline values, mean global health status did not differ between treatment groups (–4·7, 95% CI –14·8 to 5·5, p=0·36). No difference was recorded between treatment groups in 30-day mortality (absolute risk difference –0·01, 95% CI –0·14 to 0·12, p=0·89), overall mortality (–0·02, –0·17 to 0·14, p=0·84), morbidity (–0·08, –0·27 to 0·11, p=0·43), and stoma rates at latest follow-up (0·09, –0·10 to 0·27, p=0·35). However, the emergency surgery group had an increased stoma rate directly after initial intervention (0·23, 0·04 to 0·40, p=0·016) and a reduced frequency of stoma-related problems (between-group difference –12·0, –23·7 to –0·2, p=0·046). The most common serious adverse events were abscess (three in the colonic stenting group *vs* four in the emergency surgery group), perforations (six *vs* none), and anastomotic leakage (five *vs* one), and the most common adverse events were pneumonia (three *vs* one) and wound infection (one *vs* three).

Interpretation Colonic stenting has no decisive clinical advantages to emergency surgery. It could be used as an alternative treatment in as yet undefined subsets of patients, although with caution because of concerns about tumour spread caused by perforations.

Funding None.

Introduction

Colorectal cancer is a common cancer, with 412 900 new cases and 207 400 deaths in Europe in 2006.[1] 7–29% of patients with colorectal cancer present with a bowel obstruction.[2,3] Conventionally, these patients receive emergency surgery to restore luminal patency. Emergency operations are associated with mortality in 15–34% of patients and morbidity in 32–64%, despite advances in perioperative care.[3–7] Several surgical techniques can be used to treat this disorder. Usually, an ostomy is created with the intention of secondary closure, but in many patients, these ostomies will not be closed.[2,5] Patients with a permanent stoma frequently report complications and poorer health-related quality of life than do patients without colostomy.[8–11]

In the early 1990s, colonic stenting was introduced to restore luminal patency in patients with malignant obstruction of the left side of the colon. Stent placement before elective surgery, also known as a bridge to surgery, improved the clinical condition of the patient and seemed to decrease mortality, morbidity, and number of colostomies in uncontrolled studies.[5,6,12,13] Additionally, this temporary procedure enables accurate tumour staging and prevents the need for surgery in patients

with disseminated disease or unacceptable surgical risk. In these patients, the colonic stent can serve as permanent palliation. In a systematic review of 54 uncontrolled trials and case reports, self-expandable metal stents were technically successful in 91·9% of patients and clinically successful in 71·7% of patients when used as a bridge to surgery.[14] Major stent-procedure and stent-related complications were perforation (3·8%), stent migration (11·8%) and reobstruction (7·3%). The stent-procedure related mortality was less than 1%.[14] Perforation is a particular threat because it can lead to subsequent peritoneal tumour spill, changing a potentially curable disease into an incurable one.

Until now, colonic stenting has mainly been undertaken by experts in tertiary centres and published results are often retrospective or uncontrolled. Stent insertion needs to be properly assessed in randomised controlled trials.[15] We did a randomised assessment of colonic stenting versus emergency surgery, with respect to global health status, mortality, morbidity, other quality-of-life dimensions, and stoma rates.

Methods

Patients

Patients presenting with an acute left-sided colorectal obstruction presumed to be caused by a colonic malignancy were enrolled consecutively from 25 participating Dutch hospitals (four university and 21 non-university teaching hospitals). Eligible patients were aged 18 years or older, had clinical signs of severe colonic obstruction that had existed for less than 1 week, and had dilation of the colon on either plain abdominal radiograph, with typical abnormalities on a gastrografin enema study, or contrast-enhanced CT scan. The imaging modalities had to be compatible with a total or subtotal malignant colonic obstruction, and obstruction had to be located in the left side of the colon (descending colon, sigmoid, or rectum). Patients were excluded for the following reasons: signs of peritonitis, perforation, fever, sepsis, or other serious complications demanding urgent surgery; physical status of class 4 or 5 according to the American Society of Anesthesiologists; obstruction caused by a non-colonic malignancy or a benign disease; distal tumour margin of less than 10 cm from the anal verge; or inability to complete self-report quality-of-life questionnaires.

Recruitment started after the local medical ethical committees of the participating centres approved the trial. All patients provided written informed consent.

Randomisation and masking

Patients were randomly assigned (1:1 ratio) to receive colonic stenting as a bridge to surgery or emergency surgery. Computer-generated lists with random permuted blocks of size four or six per stratum were programmed by the independent Department of Clinical Epidemiology and Biostatistics of the Academic Medical Centre (University of Amsterdam, Amsterdam, Netherlands), stored centrally on a server at the Academic Medical Centre, and accessible to the local investigator through a web-based application. Stratification was by participating centre. At the moment an eligible patient gave informed consent, the local investigator called the principal investigator. The investigator logged in on the web-based application and entered the patient's details and a specific centre code. After completion of these data the randomisation result immediately appeared on the computer screen and was reported back to the local investigator.

Because of the obvious strategies under assessment, neither patients nor physicians delivering therapy and completing case record forms were masked to treatment assignment. All complications were masked for group assignment by the principal investigator and presented to PF and WAB for interpretation. The data safety monitoring committee (DSMC) assessed the interim analysis, and the final analysis was done by the study statistician and the principal investigator.

Procedures

Interventions were started within 24 h of randomisation. Colonic stenting was done by experienced endoscopists (who had placed ≥20 enteral stents including at least ten colonic stents), supported by a radiology assistant for fluoroscopy. Before colonic stenting was attempted, the distal colon was prepared with a 133 mL sodium phosphate enema. If a standard colonoscope or sigmoidoscope could traverse the lesion or the lesion seemed to be benign, stent placement was not done. Dilation of the obstructive lesion before stent placement was forbidden. Stents were placed according to the standards of the collaborative Dutch Stent-In study group.[16] If stent placement failed or symptoms of colonic obstruction did not resolve within 3 days, patients were treated surgically. Candidates for elective surgery were preferably operated on 5–14 days after inclusion, and no later than 4 weeks after inclusion. In the absence of data from published reports, the collaborative Dutch Stent-In study group decided on this timeframe on the basis that decompression should actually start directly after stent placement, but the colonic wall might take some time to recover, and time might be needed for the clinical condition of the patient to improve and adequate staging to be done. Conversely, elective surgery should not be postponed too long because of the increasing risk of stent perforation. Type and extent of surgery were selected by the treating surgeon.

In the emergency surgery group, patients were operated on according to conventional standards. In case of a primary colostomy, restoration of bowel continuity was attempted within 3–6 months.

After the initial intervention, further diagnostic work-up was done. In both treatment groups, the primary intervention was definitive if the patient refused operation (or reoperation) or had incurable metastatic disease, or

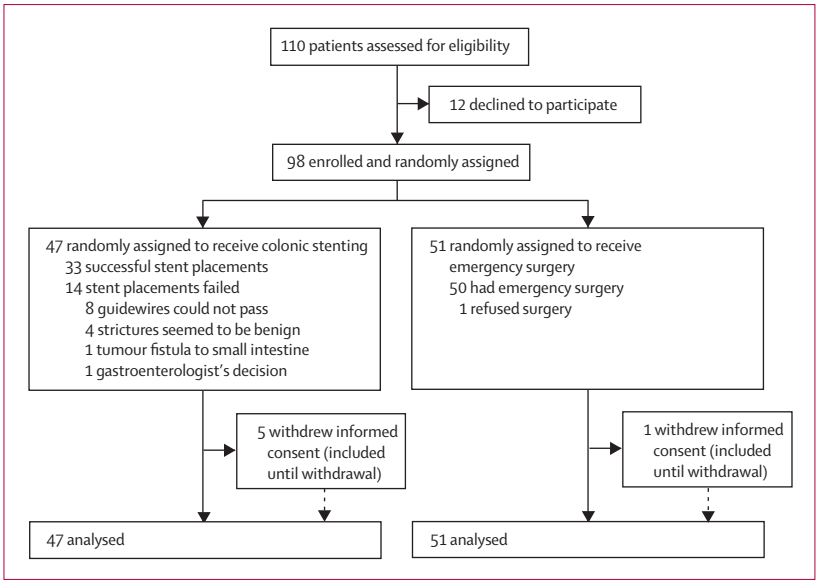

Figure 1: **Trial profile**

For the **European Medicines Agency** see http://www.emea.europa.eu

	Colonic stenting (n=47)	Emergency surgery (n=51)
Age (years)	70·4 (11·9)	71·4 (9·7)
Sex		
Men	24	27
Women	23	24
ASA classification		
Unknown	1	1
1	16	17
2	24	27
3	6	6
Severity of obstruction		
Unknown	1	1
Incomplete*	13	14
Complete†	33	36

Data are mean (SD) or number. ASA=American Society of Anesthesiologists. *Clinical signs of ileus but able to pass flatus. †Unable to pass flatus during the last 24 h before inclusion.

Table 1: **Demographic and clinical characteristics of patients at baseline**

operation (or reoperation) was judged to carry an unacceptable risk (American Society of Anesthesiologists class 4 or 5). For further specifications of the interventions, see the published protocol.[17] In accordance with the intention-to-treat principle, patients not treated according to their random assignment, irrespective of the reason, were neither crossed over nor excluded.

The primary outcome was mean global health status as assessed with the QL2 subscale of the European Organisation for Research and Treatment of Cancer (EORTC) quality-of-life questionnaire (EORTC QLQ-C30) during a 6-month follow-up.[18] This measure was chosen because the outcome of the treatments, such as need for a stoma, incisional hernia, lengthy intensive care, and hospital stay, might affect patients' quality of life.

Secondary outcomes were mortality, morbidity, other quality-of-life dimensions, and stoma rate. Mortality was assessed as procedure-related mortality within 30 days after intervention and as overall mortality during follow-up. Morbidity was defined as any event leading to hospital admission or extending hospital stay, and was assessed throughout follow-up. This description was based on the definition of a serious adverse event according to the good clinical practice guideline from the European Medicines Agency. Any untoward medical occurrences in patients other than serious adverse events were classified as other adverse events. Morbidity and other adverse events are reported together as complications.

Cancer-specific and tumour-specific quality-of-life assessments were done with EORTC QLQ-C30 and EORTC QLQ-CR38, respectively.[19] The EQ-5D questionnaire[20] was used to calculate quality-adjusted life-years in a planned cost-effectiveness analysis. After protocol publication,[17] but before start of the study, we realised that the stoma rate should have been included as an outcome because a stoma might affect quality of life and costs. Therefore, the stoma rate was added to the secondary outcomes, and was recorded at completion of the initial intervention (emergency surgery or colonic stent placement followed by surgery) and at latest follow-up.

After intervention, quality of life, mortality, morbidity, and stoma rate were assessed until death, withdrawal of informed consent, or 6-month follow-up, whichever came first. Quality-of-life questionnaires were filled out at baseline and at 4, 12, and 24 weeks after inclusion. Questionnaires, except at baseline, were mailed to the patients' homes with a stamped return envelope. During the 6-month follow-up, the research nurse contacted the patients by telephone every 2 weeks to ask about complications, reinterventions, readmissions, visits to the outpatient clinic, and missing items in the returned quality-of-life questionnaires.

Statistical analysis

The sample size was calculated with the primary outcome of global health status. With a two-group *t* test and a two-sided significance level of 0·05, we calculated that a sample size of 60 patients per group (120 patients in total) would have 80% power to detect an effect size of 0·5.[21,22] This effect size is taken as the default value for a clinically significant change on quality-of-life measures in the absence of specific information.[23] Analyses were done by intention to treat. Quality-of-life scores from available assessments during follow-up were averaged per patient, and weighted by the length of the preceding period between planned measurements.[24] Missing follow-up data were regarded as missing at random. Unless otherwise stated, differences in (weighted) quality-of-life scores between the emergency surgery and colonic stenting groups were assessed for statistical significance by

	Colonic stenting*		Emergency surgery†		Between-group difference‡	p value
	Baseline (n_{max}=40)	Follow-up (n_{max}=39)	Baseline (n_{max}=42)	Follow-up (n=44)		
Global health status§	34·0 (23·2)	63·0 (23·8)	42·5 (28·0)	61·4 (21·9)	−4·7 (−14·8 to 5·5)	0·36
Functional scales§						
Physical	67·5 (31·3)	67·9 (28·7)	75·4 (28·8)	68·9 (24·1)	0·2 (−11·5 to 11·9)	0·98
Role	39·6 (39·2)	55·5 (30·0)	55·6 (37·8)	57·6 (29·0)	1·0 (−13·3 to 15·4)	0·88
Emotional	57·7 (26·8)	78·3 (23·5)	62·1 (23·3)	78·2 (21·6)	−2·2 (−11·7 to 7·2)	0·64
Cognitive	71·7 (27·0)	82·5 (23·9)	75·0 (22·2)	81·3 (17·8)	−2·0 (−11·6 to 7·5)	0·67
Social	62·1 (33·1)	76·3 (25·2)	68·7 (33·0)	70·8 (25·8)	−7·5 (−18·7 to 3·7)	0·19
Symptom scales§						
Fatigue	61·7 (33·9)	42·0 (26·4)	57·0 (30·9)	40·2 (22·9)	−1·6 (−13·1 to 9·8)	0·78
Nausea and vomiting	57·1 (34·8)	18·8 (25·7)	48·4 (36·2)	11·6 (16·0)	7·6 (−9·9 to 25·2)¶	0·39
Pain	72·5 (30·6)	20·9 (24·7)	61·9 (32·6)	18·7 (22·7)	−1·5 (−12·3 to 9·4)	0·79
Dyspnoea	25·0 (30·0)	17·5 (26·4)	20·6 (28·5)	16·9 (25·2)	−0·9 (−12·6 to 10·8)	0·88
Insomnia	60·8 (38·4)	23·6 (30·0)	44·4 (38·7)	25·4 (27·7)	−3·1 (−15·9 to 9·7)	0·63
Appetite loss	69·2 (31·5)	21·2 (30·5)	60·3 (39·8)	24·6 (26·2)	5·6 (−7·4 to 18·7)	0·39
Constipation	86·3 (23·8)	12·3 (26·3)	84·1 (28·7)	6·6 (11·4)	−3·9 (−12·2 to 4·4)	0·36
Diarrhoea	20·0 (32·7)	13·2 (18·7)	14·3 (25·7)	11·6 (18·5)	−3·2 (−11·8 to 5·4)	0·46
Financial difficulties	3·3 (10·1)	11·8 (23·8)	3·3 (12·5)	8·1 (19·6)	−2·1 (−11·5 to 7·4)	0·67

Data are mean (SD) or mean difference (95% CI). n_{max}=maximum number of patients with available data. *39–40 patients had data at baseline, 37–39 patients had data at follow-up, and 34–36 patients had data at baseline and follow-up. †41–42 patients had data at baseline, 44 patients had data at follow-up, and 38–39 patients had data at baseline and follow-up. ‡Value for emergency surgery during follow-up minus colonic stenting during follow-up, based on estimated marginal means with baseline values as covariates; n_{max}=36 patients for colonic stenting and n_{max}=39 for emergency surgery. §Higher scores on the global health status and functional scales indicate higher quality of life; higher scores on the symptom scales indicate lower quality of life. ¶Difference represents the change in scores from baseline to follow-up in the emergency surgery group minus the colonic stenting group because of violation of the assumption of equality of error variances in the covariance analysis.

Table 2: **Differences in quality of life during follow-up between patients receiving colonic stenting and emergency surgery, according to EORTC-QLQ-C30, based on available data and corrected for differences at baseline**

analysis of covariance to adjust for baseline scores. Differences in procedure-related mortality (at 30 days), overall mortality, morbidity, and stoma rates were assessed by the χ^2 test. Differences in survival were assessed by the Kaplan-Meier log-rank test. All reported p values are two-sided and were judged to be significant at less than 0·05. Analyses were done with SPSS (version 18.0).

The DSMC safeguarded the trial patients with respect to safety and effectiveness. Morbidity and mortality in the experimental group (colonic stenting) was reported to the DSMC on short notice. An interim analysis was scheduled for after the first 60 treated patients completed 30 days of follow-up. No formal stopping rule was formulated beforehand.

This study is registered, number ISRCTN46462267.[17]

Role of the funding source

There was no funding source for this study. The corresponding author and MGD had full access to all the data and the corresponding author had final responsibility to submit for publication.

Results

Between March 9, 2007, and Aug 27, 2009, 98 patients (mean age 71·0 years [SD 10·8]) were enrolled from 25 centres and randomly assigned to receive colonic stenting or emergency surgery (figure 1). Demographic and clinical characteristics were balanced between treatment groups at baseline (table 1). Two protocol violations occurred. One patient refused emergency surgery and was treated with a colonic stent followed by uneventful elective surgery. One endoscopist refused to do endoscopy because of uncertainty about the malignant nature of the stricture; this patient received emergency surgery, which was complicated by three events (two graded as morbidity); the pathology report showed a malignant obstruction.

60 patients had been enrolled by Feb 20, 2009, and had completed 30 days of follow-up by March 23, 2009. Before the planned interim analysis was finalised, substantial morbidity and some mortality occurred in the colonic stenting group. The DSMC was informed and requested an additional analysis as soon as 90 patients had completed the first month of their follow-up. The study was put on hold on Sept 18, 2009, after 98 patients had been enrolled, because the DSMC suspected that morbidity was higher in the colonic stenting group than the emergency surgery group. An independent statistician and the principal investigator analysed the data limited to 30 days of follow-up. The analyses done for 60 and 90 patients did not show significant differences between the treatment groups for in-hospital mortality or 30-day mortality. However, the colonic stenting group was associated with an increased number of patients with

	Colonic stenting (n=47)	Emergency surgery (n=51)	Absolute risk difference (95% CI)	Relative risk (95% CI)	p value
Mortality					
30-day mortality	5	5	–0·01 (–0·14 to 0·12)	0·92 (0·28 to 2·98)	0·89
Overall mortality	9	9	–0·02 (–0·17 to 0·14)	0·92 (0·40 to 2·12)	0·84
Morbidity*	25	23	–0·08 (–0·27 to 0·11)	0·85 (0·57 to 1·27)	0·43
Stoma rates					
Directly after initial intervention	24	38	0·23 (0·04 to 0·40)	1·46 (1·06 to 2·01)	0·016
At latest follow-up	27	34	0·09 (–0·10 to 0·27)	1·16 (0·85 to 1·59)	0·35

Data are number unless otherwise indicated. *Number of patients who had an extended hospital stay or at least one additional hospital admission.

Table 3: **Secondary outcomes (intention-to-treat population)**

events graded as morbidity at 30-day follow-up, with an absolute risk increase of 0·19 (95% CI –0·06 to 0·41; relative risk 1·60, 95% CI 0·85 to 3·01) in the interim analysis of 60 patients (14 of 28 patients receiving colonic stenting *vs* 10 of 32 receiving emergency surgery), and an absolute risk increase of 0·19 (–0·01 to 0·37; relative risk 1·62, 0·94 to 2·78) in the interim analysis of 90 patients (23 of 47 patients *vs* 13 of 43). After consultation with an independent external expert, the DSMC felt obliged to stop the trial definitively. The trial was officially ended on March 12, 2010.

In analysis of the primary outcome, we recorded no difference in global health status between the treatment groups (table 2). Furthermore, we recorded no differences in the secondary outcomes of mortality and morbidity between study groups (table 3). The most common serious adverse events were abscess, perforation, and anastomotic leakage, and the most common adverse events were pneumonia and wound infection (table 4). We did not record any significant differences in cancer-specific quality of life (table 2) or tumour-specific quality of life (table 5) between the treatment groups, except for more stoma-related problems in the colonic stenting group than in the emergency surgery group (table 5). Directly after the initial intervention, significantly more patients in the emergency surgery group had a stoma (table 3). Restoration of bowel continuity was achieved in two of 24 patients in the colonic stenting group and in five of 38 patients in the emergency surgery group. Anastomotic leakage led to five additional stomata in the colonic stenting group and one additional stoma in the emergency surgery group. At the latest follow-up, 27 patients receiving colonic stenting and 34 receiving emergency surgery still had a stoma (table 3).

In all patients allocated to receive colonic stenting, with the exception of one protocol violation, an attempt to place the stent was made within 24 h of randomisation. Dilation of the malignant stricture was not done before or after stent placement, and forced passage of the stricture by the endoscope was not reported in any patients. Stent placement was technically successful in 33 of 47 patients (figure 1). In eight patients a guidewire could not be passed along the colonic stricture, four patients seemed to have a benign stricture, one patient had a tumour fistula to the small intestine, and one protocol violation, described above, occurred.

27 patients received one stent and six patients received two stents during the initial stent placement procedure. In

	Colonic stenting (n=47)	Emergency surgery (n=51)
Patients with morbidity*	25	23
Abscess	3	4
Perforation		
Guidewire perforations	2	0
Stent-related perforations	4	0
Anastomotic leakage	5	1
Respiratory insufficiency	3	2
Wound dehiscence	2	2
Electrolyte disturbance	1	2
Sepsis	0	3
Wound infection	2	1
Bleeding	0	2
Ileus	0	2
Constipation	2	0
Organ failure	1	1
Epileptic insult	0	1
Embolism	0	1
Myocardial infarction	0	1
Patients with other adverse events†	8	12
Pneumonia	3	1
Wound infection	1	3
Delirium	2	1
Gastroparesis	0	3
Urinary-tract infection	0	2
Perforation	0	1
Electrolyte disturbance	0	1
Abscess	1	0
Embolism	1	0

*Any event leading to hospital admission or extension of hospital stay (serious adverse event). †Adverse events other than serious adverse events.

Table 4: **Patients with complications**

	Colonic stenting*		Emergency surgery†		Between-group difference‡	p value
	Baseline (n_{max}=39)	Follow-up (n_{max}=38)	Baseline (n_{max}=40)	Follow-up (n_{max}=44)		
Functional scales§						
Body image	76·9 (23·8)	74·5 (23·6)	73·0 (30·8)	74·6 (24·8)	−1·4 (−10·8 to 8·0)	0·77
Future perspective	43·0 (35·4)	58·2 (29·4)	41·9 (34·8)	59·4 (27·9)	−2·9 (−15·7 to 10·0)	0·66
Sexual functioning	13·7 (20·7)	13·1 (18·6)	12·0 (20·8)	10·6 (15·8)	−1·5 (−10·7 to 7·6)	0·74
Sexual enjoyment	35·7 (38·0)	41·6 (39·0)	36·7 (36·7)	28·8 (31·6)	−17·6 (−56·5 to 21·3)	0·34
Symptom scales§						
Micturition problems	29·2 (19·1)	30·5 (13·0)	22·5 (20·8)	27·1 (14·0)	−4·5 (−10·8 to 1·9)	0·17
Chemotherapy side-effects	39·5 (28·2)	25·6 (22·7)	35·3 (20·8)	25·2 (19·4)	0·9 (−9·4 to 11·2)	0·87
Gastrointestinal problems	49·9 (15·3)	15·3 (13·9)	40·9 (20·1)	15·7 (13·4)	1·2 (−5·2 to 7·6)	0·71
Male sexual functioning¶	21·6 (28·1)	25·8 (30·6)	34·4 (42·5)	40·7 (36·3)	5·0 (−13·3 to 23·2)	0·59
Defecation problems	24·2 (15·9)	12·9 (10·3)	22·7 (15·6)	9·2 (6·4)	−3·2 (−10·2 to 3·7)	0·35
Stoma-related problems	..	40·5 (22·6)	..	28·6 (19·6)	−12·0 (−23·7 to −0·2)‖	0·046
Weight loss	45·0 (36·2)	30·8 (29·5)	37·6 (35·2)	25·0 (22·6)	−8·5 (−20·7 to 3·8)	0·17

Data are mean (SD) or mean difference (95% CI). n_{max}=maximum number of patients with available data. *14–39 patients had data at baseline, 17–38 had data at follow-up, and 7–34 patients had data at baseline and follow-up; reduced numbers of patients with available data resulted from non-response to questionnaire items on sexual enjoyment or defecation problems. †10–40 patients had data at baseline, 16–44 patients had data at follow-up, and 6–38 patients had data at baseline and follow-up; reduced numbers of patients with available data resulted from non-response to questionnaire items on sexual enjoyment or defecation problems. ‡Value for emergency surgery during follow-up minus colonic stenting during follow-up, based on estimated marginal means with baseline values as covariates; n_{max}=34 for colonic stenting and n_{max}=38 for emergency surgery. §Higher scores on the functional scales indicate higher quality of life; higher scores on the symptom scales indicate lower quality of life.¶Data for female sexual functioning are not presented because too few female patients had data at baseline (four each in the colonic stenting and emergency surgery groups), follow-up (four in the colonic stenting group, three in the emergency surgery group), and baseline and follow-up (one each in the colonic stenting and emergency surgery groups). ‖Differences in stoma-related problems in 21 patients receiving colonic stenting and 32 receiving emergency surgery are reported for follow-up only.

Table 5: **Differences in quality of life related to colon cancer during follow-up between patients receiving colonic stenting and emergency surgery, according to EORTC-QLQ-CR38, based on available data and corrected for differences at baseline**

total, 31 enteral Wallstents (Boston Scientific, Natick, MA, USA; diameter 22 mm) and eight WallFlex colonic stents (Boston Scientific, Natick, MA, USA; diameter 25 mm) were placed. 24 stents were 6 cm and 15 were 9 cm in length. In all patients who received a colonic stent, the obstruction clinically resolved, leading to a clinical success of 70%. A procedure-related perforation occurred in two patients and a stent-related perforation occurred in four patients (table 4).

In total, 110 operations were done by a general surgeon (20, 18%) or a colorectal surgeon (87, 79%), and in three cases (3%) the surgeon was not traceable. Ultimately, 78 surgeons did between one and six operations within this trial.

In the colonic stenting group, surgery was done in 31 of 33 patients who underwent technically and clinically successful stent placement, whereas the stent served as palliative treatment for the remaining two patients. These operations were done by colorectal surgeons in 23 of 31 cases. In 20 patients, a primary anastomosis was attempted, which succeeded in 15 patients. In three operative specimens, silent stent perforation was detected. Across the full colonic stenting group, 52 operations were done, 41 by colorectal surgeons. A primary anastomosis was attempted in 21 patients, but in five patients an anastomotic leakage occurred. Additionally, a definitive stoma was applied in seven patients, and a temporary stoma was applied in 17 patients, two of whom subsequently had bowel continuity restored.

All patients in the emergency surgery group, with the exception of one protocol violation, were operated on within 24 h of randomisation. 41 of 50 emergency operations were done by a colorectal surgeon. A primary anastomosis was achieved in 12 patients (succeeded in 11), a temporary stoma was done in 25 patients, and a definitive stoma was done in 13 patients.

Eight additional operations were done: one primary anastomosis in the patient who had received a colonic stent instead of emergency surgery; four restorations of bowel continuity in one attempt, and one restoration in two attempts; and one stoma creation because of an anastomotic leakage. Pathological examination showed that in four of 51 patients the stricture was of benign origin.

Discussion

In this multicentre randomised trial, colonic stenting or emergency surgery did not have any distinct benefits for global health status, mortality, morbidity, other quality-of-life dimensions, and stoma rates. These results are less favourable than are previous data obtained from comparative non-randomised,[4,5,13] matched controlled,[6,12] and non-comparative studies[14,25] (panel).

We might have selected a population at increased risk for complications: 70% of patients presented with a

Panel: Research in context

Systematic review

We searched PubMed, Embase, and the Cochrane Library from January, 1990, to January, 2006, for relevant articles by use of the search terms "colon" or "colorectal", "cancer" or "malignant", "acute obstruction" or "stenosis", "stent" or "stenting", "emergency surgery" or "operation", and "randomised" or "controlled trial". All languages were included. Because no randomised controlled trial could be identified, high-grade evidence seemed to be lacking. During preparation of this report, the first randomised controlled trial of colonic stenting versus emergency surgery was published.[26]

Interpretation

Our trial is, to our knowledge, the largest randomised trial of colonic stenting as a bridge to surgery versus emergency surgery for allcomers with left-sided malignant colonic obstruction in university and non-university teaching hospitals. In this setting, colonic stenting has no decisive clinical advantages to emergency surgery. These findings are consistent with the only other randomised controlled trial in this setting.[26] Moreover, both trials raise concerns regarding overt and silent perforations. Further studies are needed to increase data on oncological outcomes and to identify specific subgroups of patients who might benefit from colonic stenting or emergency surgery.

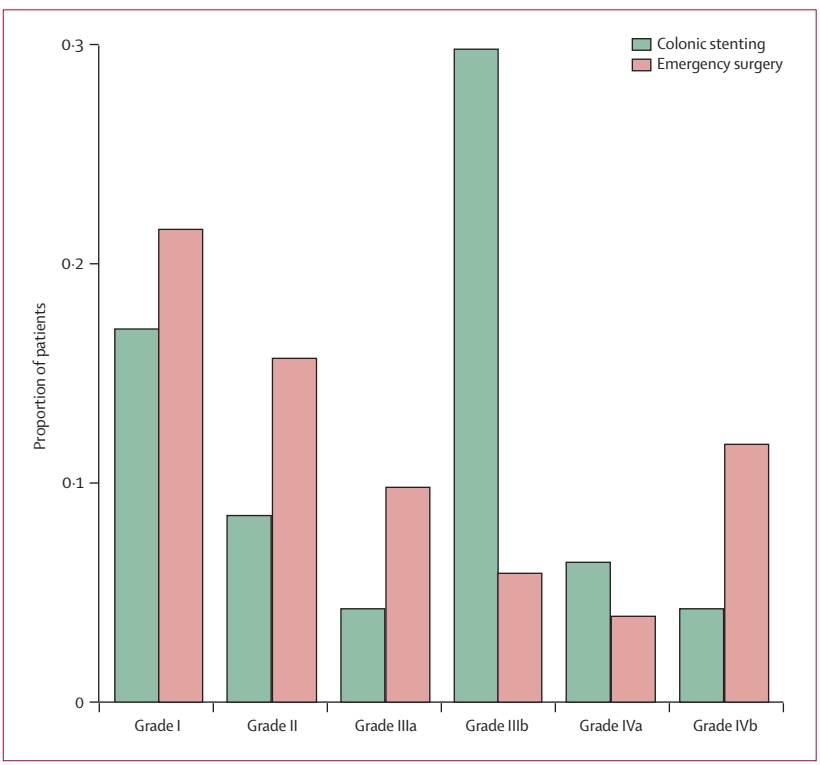

Figure 2: **Clavien-Dindo classification of complications**[28]

complete obstruction, which is high in comparison with published data (53·8%).[25] In patients with a total obstruction, stent placement is more difficult[27] and the bowel might be less easily decompressed than in patients with incomplete obstruction, and, therefore, the condition of these patients could be suboptimum at time of surgery, resulting in a fairly high leak rate if resection without a stoma is attempted. In a retrospective study from a renowned tertiary referral centre, complete obstruction has been identified as a risk factor for complications.[25]

The quite high morbidity in our study might also originate from the meticulous survey of complications with telephone calls every 2 weeks during a 6-month period and a strict definition of morbidity. In addition to complications of the initial intervention, we also included complications that occurred because of subsequent elective operations and all events that led to readmission within 6-month follow-up. In most published studies with a less strict follow-up, the morbidity rate is probably underestimated. To increase our understanding of the severity of the complications, we redefined them according to the Clavien-Dindo classification, a frequently used classification system for surgical complications (figure 2).[28]

Existing data on colonic stenting as a bridge to surgery focuses on technical success, clinical success, complications related to placement of the stent, and complications related to presence of the stent in the colon.[5,12,14,25] Our technical success of 70% was rather low compared with the published data (91·9%).[14] Although we requested expert guidance for stent placement, a guidewire could not be passed along the colonic stricture in eight patients. All endoscopists in our trial were experienced in pancreaticobiliary endoscopy, and, therefore, are proficient in colonic stenting,[25] possibly because they are used to passing guidewires along strictures, work with catheters and contrast, and are familiar with the placement of metal stents albeit in the biliary tract. The fairly high number of patients with a complete obstruction might also have lowered the technical success. However, our clinical success was in accordance with published data.[14]

Findings of published reports show procedure-related and stent-related complications in 5–23·1% of patients, with an average of stent-related perforations in 5%.[5,12,14,25] In our population, two (4%) procedure-related and four (9%) stent-related complications occurred. We were very surprised by the high number of colonic specimens showing signs of silent colonic perforation by the prosthesis, which increased the total percentage of colon perforations to almost 20% (nine perforations in 47 patients). Pirlet and colleagues[26] reported two stent perforations and eight silent perforations in 30 patients randomised to colonic stenting as a bridge to surgery. The oncological consequences of potential tumour dissemination caused by perforations are unclear, but the possibility of dissemination is worrisome and these silent

perforations should not be disregarded.[26] The consequences of dissemination could perhaps be derived from survival data. However, data from non-randomised studies are inconsistent, ranging from no difference between colonic stenting and emergency surgery to a significantly reduced 5-year survival for patients treated with colonic stenting before elective surgery.[6,29]

Another frequently used outcome to assess treatments for colonic obstruction is number of ostomies.[5,12] In our trial, stoma rate was significantly lower in the colonic stenting group than in the emergency surgery group after initial intervention, but this difference had disappeared by the end of follow-up. The difference was partly caused by the high leakage rate of primary anastomosis in the stenting group, probably because bowel decompression and improvement of the patients' clinical condition were insufficient at the time of elective operation. Additionally, the elective nature of the operation and the surgeons' faith in the idea of bridge to surgery might have made the surgeons less conservative than in the emergency surgery group. Maybe we should have lengthened the interval between stent placement and elective surgery. The type of surgeon is unlikely to have affected stoma rate because all patients in whom a leakage occurred, with the exception of one, were operated on by a colorectal surgeon. The low restoration rate of bowel continuity might have been caused by the start of chemotherapy in most of our patients directly after initial intervention, which might have delayed reoperation until after the completion of the trial.

How do our data compare with those in other studies? Unfortunately, the primary endpoint cannot be compared because we were the first to use quality of life as an outcome measure in this setting. With respect to mortality, findings of a randomised trial[26] and several comparative non-randomised or matched controlled studies did not show a significant difference between colonic stenting and emergency surgery,[4–6,12] with the exception of a study by Park and colleagues.[13] Morbidity seemed to be in favour of the stenting group in two studies.[6,13] With respect to stoma rate, significantly more primary anastomosis was recorded in the stenting group than in the emergency surgery group in non-randomised studies.[4–6,12] By contrast, in the randomised trial, 17 of 30 patients in the emergency surgery group and 13 of 30 patients in the colonic stenting group sustained a stoma (p=0·30).[26]

Our study design has some shortcomings. First, quite a large number of hospitals actively recruited patients, ranging from one to 17 patients per centre. While designing the study, we considered limiting enrolment and endoscopic treatment to tertiary referral centres, but this restriction would have made the results unsuitable for translation to clinical practice. Second, in the emergency surgery group, all but one of the patients received the allocated treatment, whereas six patients in the colonic stenting group did not seem to have an indication for stent placement (figure 1). In the four patients in whom the lesion seemed to be benign at endoscopy, the procedure was ceased and endoscopists did not attempt to place the stent. Because of frail evidence of the benefit of stenting in benign colonic strictures, and the likelihood of a high occurrence of complications in patients with acute diverticular disease who receive a colonic stent,[30] we aimed to exclude these patients from our population by requiring sound images of the colon before enrolment. However, we could not achieve complete exclusion of patients with benign colonic strictures without pathological confirmation before stent placement, and such confirmation was, in our opinion, not feasible because of the importunate character of an acute colonic obstruction. Therefore, we reasoned that refraining from stent placement in these patients would be best.

Third, a cost-effectiveness analysis, including costs per quality-adjusted life-year as an outcome measure, was planned alongside this randomised trial. In view of advice from the DSMC, we decided to refrain from judgment about the economic viability of colonic stenting when safety was possibly at stake. Last, our trial was ended early, implying a loss of statistical power because the sample size was smaller than expected. However, the similarity in global health status, mortality, morbidity, other quality-of-life dimensions, and stoma rates between treatment groups suggests that the probability of colonic stenting becoming more effective than emergency surgery is negligible.

The findings of this randomised trial did not show that colonic stenting as a bridge to surgery was better than emergency surgery for all comers with left-sided malignant colonic obstruction in university and non-university teaching hospitals. Our data cannot be extrapolated to specific groups of patients—eg, those at high risk of complications from operations because of old age or obesity, or those with colonic obstruction of low severity—or to expert centres in colonic stent placement. In our opinion, colonic stenting can be used as an alternative to emergency surgery, but should be used with caution, mainly because of concerns of overt and silent perforations. Future studies need to further investigate oncological outcomes and establish whether specific groups of patients could have a greater benefit from either colonic stenting or emergency surgery.[25]

Contributors

JEvH participated in the study co-ordination, and data collection and analysis. MGD and MAS participated in the study design and data analysis. BO participated in the study design, and BO, AWM, MFLH, MJG participated in the inclusion and treatment of patients. WAB and PF initiated the study, and participated in the study design and treatment of patients. JEvH, WAB, MAS, MGD, and PF participated in writing of the report; and BO, AWM, MFLH, and MJG reviewed the report.

Conflicts of interest

BO's institution has received research grants from Abbott, Merck Sharp and Dohme, and Ferring; and BO has received payment for lectures from Abbot. PF's institution has received research grants from Olympus Medical Systems, Boston Scientific, and Cook Endoscopy; and PF has been a consultant for Ethicon Endosurgery, Covidien, Cook Endoscopy, and Torax Medical. All other authors declare that they have no conflicts of interest.

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