Combined endoscopic laparoscopic surgical treatment of advanced adenomas and early colon cancer

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ABSTRACT

INTRODUCTION: A subgroup of patients with benign colonic neoplasia is unsuitable for standard endoscopic treatment modalities. These patients may benefit from a combined endoscopic and laparoscopic surgical (CELS) approach. A CELS procedure may even be an option for some patients with a small malignant lesion where resection of the colon may be associated with an excessively high risk of procedure-related morbidity and mortality.

METHODS: All patients considered for a CELS procedure were evaluated at a multidisciplinary team conference. The CELS procedures were performed as laparoscopy-assisted endoscopic mucosal resections or endoscopy-assisted laparoscopic resections.

RESULTS: A total of 25 patients were included. Five patients had a malignant and 20 patients had a benign lesion. Two patients with histologically verified malignant lesions preoperatively had CELS performed due to severe co-morbidity. In one patient with initially benign biopsies, the resected CELS specimen revealed adenocarcinoma. This patient subsequently underwent oncological resection (no residual disease). In the last two cases, the lesions were assessed during CELS and they exhibited endoscopically malignant features. Consequently, both patients underwent immediate oncological segmental colon resection.

CONCLUSIONS: CELS is a feasible treatment for colonic neoplasia where endoscopic resection alone is not technically possible. In case of severe co-morbidity ruling out segmental resection in patients diagnosed with T1 or T2 colorectal cancer, CELS treatment may be considered.

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During the past couple of decades, endoscopic as well as laparoscopic techniques have evolved significantly, and the modalities for treatment of patients with colonic neoplasia have changed dramatically [1].

Furthermore, there is a growing demand for individually tailored treatment for challenging patients. A proportion of patients with benign colonic neoplasia are unsuitable for endoscopic removal due to difficulty in visualising the lesion, in maintaining a stable position of the endoscope during the intervention, or due to a high risk of perforation. Commonly, the treatment recommendation for these patients has been segmental colectomy, with the ensuing risk of complication. A procedure that combines laparoscopy and endoscopy may be used to avoid bowel resection and minimise the length of stay in hospital [2-4]. This procedure is commonly coined combined endoscopic and laparoscopic surgery (CELS) [5, 6]. A CELS procedure could be a safe alternative to standard resection in patients with severe co-morbidity and small early detected cancer without clinical signs of local or systemically advanced disease.

The aim of the present study was to determine the safety and feasibility of the CELS procedure.

METHODS

All patients scheduled for a CELS procedure from April 2016 to May 2017 were included in the study. The data were collected retrospectively from hospital records. Data included patient age, gender, American Society of Anesthesiologists class, BMI, Zubrod score, operative time, polyp characteristics, indication, length of stay and procedures.

Patients were selected for CELS based on various criteria, including large polyp size or "non-lifting" sign, difficult polyp location or severe co-morbidity excluding the patient from standard bowel resection. All candidates for CELS were evaluated at a multidisciplinary team (MDT) conference involving expert endoscopists and colorectal surgeons, and also a radiologist, an oncologist and a pathologist if a diagnosis of a malignant lesion had already been established. Prior to the MDT conference, all patients underwent full colonoscopy and all lesions were evaluated by an expert endoscopist during the colonoscopy. Video recordings and/or still pictures of the lesions were presented at the MDT conference. A thoracoabdominal CT was performed if malignancy was present or suspected preoperatively.

ORIGINAL ARTICLE

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FIGURE 1

Illustration of suggested set-up for left colon lesion.

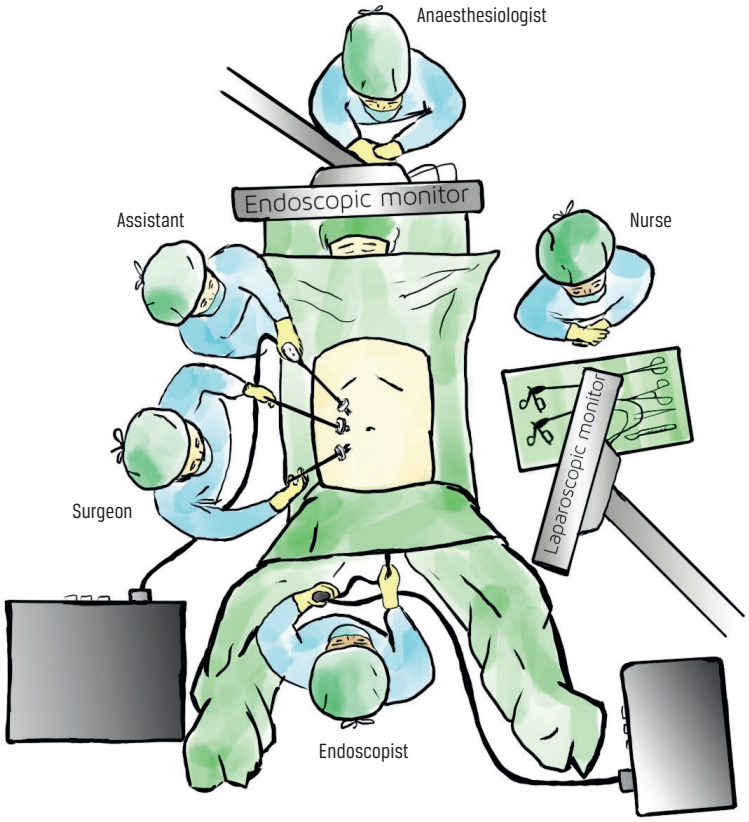
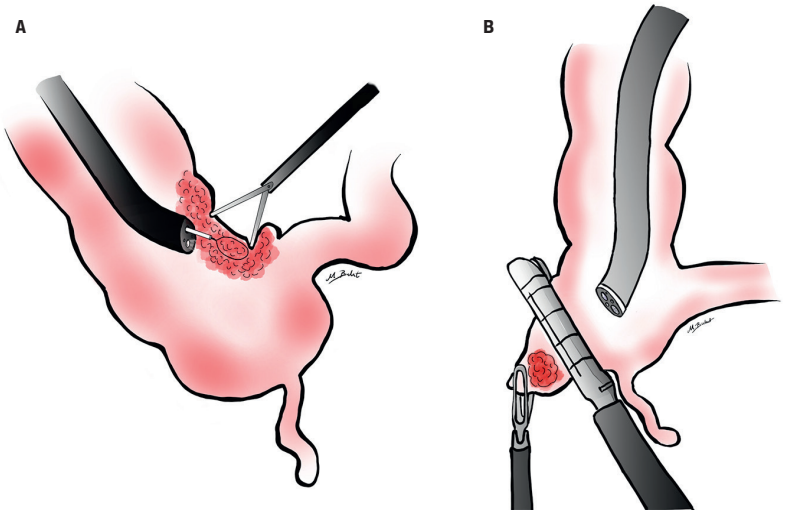


FIGURE 2

Illustration of combined endoscopic and laparoscopic surgical approach. Laparoscopically assisted endoscopic mucosal resections (**A**) and endoscopically assisted laparoscopic resections (**B**).



Surgical technique

All patients underwent a standard bowel cleansing prior to the CELS procedure.

Patients were placed in supine split-leg or lithotomy position with subsequent establishment of general anaesthesia, orogastric tube and urinary catheter. Pneumoperitoneum was established, and the laparoscopy initiated while colonoscopy was performed. Laparoscopic monitors were placed on the same side as the colonic lesions, whereas the endoscopic monitor was positioned at the head. The surgeon and his assistant were positioned on the opposite site of the colonic lesion and the endoscopist was situated between the patient's legs (**Figure 1**).

CELS procedures were performed either as laparoscopically assisted endoscopic mucosal resections (EMR) or as endoscopically assisted laparoscopic resections (**Figure 2**). If the laparoscopically assisted approach was chosen, the serosa was monitored carefully during the endoscopic mucosal resection which made it possible to change the position of the colon and thereby improve endoscopic access to the lesion. If any full-thickness thermal injury or perforation should occur, seromuscular sutures could be placed laparoscopically. This possibility of bowel repair allowed the endoscopist to perform a more radical mucosal resection. If endoscopic mucosal resection was insufficient due to a non-lifting area, the area was removed by sleeve stapling. When endoscopically assisted CELS was performed, the endoscopist pinpointed the lesion and sleeve stapling was performed with the endoscopist monitoring the procedure from inside, thus securing adequate surgical margins to the lesion. At the end of the procedure, an air-leak test was performed to ensure an intact stapling line.

The patient and the CELS team were prepared for conversion to laparoscopic segmental colon resection if the lesion was not suitable for sleeve resection or if the lesion, originally estimated to be of a benign nature, was suspected to be malignant during the CELS procedure.

The stapled specimens were sent for histopathological evaluation pinned onto a corkboard.

Statistics

Continuous variables are presented as median and range under the assumption that data are not normally distributed. Categorical variables are presented as frequencies.

Ethical considerations

Trial registration: This study was assessed by The National Committee on Health Research Ethics (SJ-593), which concluded that the study required no approval from the Committee. The study was approved by the Danish Data Protection Agency (REG-126-2017).

RESULTS

Twenty-five patients were treated with a CELS procedure in the study period. Patient demographics and characteristics of the cohort are shown in **Table 1**. In total, 20 patients had a benign lesion and five patients had a malignant lesion either on their prior endoscopy or on subsequent pathology.

Detailed descriptions of individual patients are outlined in **Table 2**.

All endoscopically assisted laparoscopic resections resulted in specimens with free resection margins.

Endoscopic evaluation six months after the laparoscopically assisted EMR procedures revealed one patient (patient no. 18) with a small residual adenoma, whereas the other six had no sign of adenoma at the resection site.

There were no cases where laparoscopic bowel repair was needed during laparoscopically assisted CELS. The median polyp size of the benign lesions was 30 mm (10-80 mm); for malignant lesions, the median size was 17 mm (15-70 mm). The median operative time for endoscopically assisted CELS and laparoscopically assisted CELS were 70 min. (44-177 min.) and 79 min. (54-114 min.), respectively.

The median length of stay in hospital was one day after laparoscopically assisted EMR and one day after endoscopically assisted laparoscopic resection.

Seven patients had laparoscopically assisted EMR, 12 patients had endoscopically assisted laparoscopic resection, two patients had both, and the CELS procedure was converted to laparoscopic colon resection in three patients.

Nineteen cases had a benign histology and completed CELS. In 15 cases, no residue in the follow-up colonoscopy within six months was observed. In one case, there was a small residue < 5 mm with low-grade dysplasia (patient no. 19) and the patient did not want further treatment. Patient no. 11 was referred to another hospital due to histology with mucinous neoplasm and their follow-up showed no residue and no need for further treatment. One patient did not want follow-up, and one patient is awaiting colonoscopy.

In two out of 25 patients (patients no. 2 and 9), the lesions were known to be malignant preoperatively, but CELS was performed due to severe co-morbidity. Patient no. 2 had severe chronic obstructive pulmonary disease, ischaemic heart disease, coronary stent, spinal stenosis, BMI = 46 kg/m^2, Zubrod performance status level 2 and Mantle cell lymphoma and had just ended radical radiation therapy for a T1 pulmonary cancer. Although the operative time was only 45 min., the patient had markedly elevated cardiac troponins post-operatively but no other signs of myocardial infarction. Patient no. 9 was an 85-year-old male with ischaemic heart disease, coronary stent, diabetes mellitus Type 2, hypertension and Zubrod performance status level 2.

TABLE 1

Patient demographics and characteristics, N = 25.

Age, median (range) yrs	71 (36-88)
Sex, n (%)	
Female	12 (48)
Male	13 (52)
ASA class, n (%)	
I	3 (12)
II	14 (56)
III	8 (32)
BMI, median (range), kg/m^2	29 (20-46)
Operative time, median (range) min.	
Endoscopically assisted CELS	70 (44-177)
Laparoscopically assisted CELS	79 (54-173)
Laparoscopic segmental resection	172 (163-191)
Polyp size, median (range), mm	
Benign	30 (10-80)
Malignant	17 (15-70)
Length of stay, median (range), days	
Endoscopically assisted CELS	1 (0-16)
Laparoscopically assisted CELS	1 (0-3)
Laparoscopic segmental resection	5 (4-12)

ASA = American Society of Anesthesiologists; CELS = combined endoscopic and laparoscopic surgery.

Three additional patients turned out to have malignant lesions. One patient (no. 7) with preoperative benign biopsies underwent oncological resection with hemicolectomy 22 days after the CELS procedure in which a T3-adenocarcinoma was resected. Histopathological examination of the colonic resection specimen demonstrated no residual tumour and there were no signs of metastatic disease, T3N0M0.

In one patient (no. 8), a colonic lesion was seen on a CT, but the lesion could not be reached endoscopically due to a large inguinal hernia containing the sigmoid colon. During CELS, the hernia was reduced laparoscopically and the lesion was reached. Endoscopic assessment revealed a malignant lesion, and oncological right-sided hemicolectomy was performed. The pathological assessment revealed a pT3N0M0 adenocarcinoma.

One patient (no. 23) who had benign biopsies upon initial endoscopy turned out to have obvious malignancy when reassessed during the CELS procedure. Consequently, an oncological right-sided hemicolectomy was performed. Histopathology confirmed the diagnosis of adenocarcinoma, T3N0M0.

In one patient (no. 10) with benign histology, a laparoscopically assisted EMR was performed leaving a small non-lifting area. Because the lesion was facing the retroperitoneum and because of severe co-morbid-

TABLE 2

Results.

Patient no.	Indication	Size, mm	Histology before CELS	Location	Procedure	Histology	LOS, days
1	Non-lifting polyp	50	Adenoma LGD	Caecum	Stapling	Adenoma HGD	3
2	Co-morbidity	17	Adenocarcinoma	Ascending colon	Stapling	Adenocarcinoma, pT1NxM0	3
3	Non-lifting polyp	80	Adenoma LGD	Caecum	EMR	Adenoma HGD	1
4	Non-lifting polyp	15	Sessile serrated lesion	Caecum	EMR + stapling	Sessil serrated adenoma	3
5	Size and location	70	Adenoma LGD	Ascending colon	EMR	Adenoma LGD	3
6	Anatomical location	30	Adenoma LGD	Caecum	Stapling	Adenoma LGD	1
7	Non-lifting polyp	17	Adenoma HGD	Ascending colon	Stapling	Adenocarcinoma, pT3NxM0	2
8	CT-verified pathology	70	None	Ascending colon	Lap. surgery	Adenocarcinoma, pT3N0M0	5
9	Co-morbidity	25	Adeno-carcinoma	Ascending colon	Stapling	Adenocarcinoma, pT2NxM0	1
10	Non-lifting polyp	20	Adenoma LGD	Splenic flexure	Aborted	–	0
11	Anatomical location	35	Non-specific reactive tissue	Appendiceal orifice	Stapling	Low grade mucinous neoplasm	1
12	Non-lifting polyp	10	Sessile serrated lesion	Splenic flexure	EMR	Adenoma LGD	0
13	Anatomical location	16	Adenoma LGD	Ileocecal valve	EMR	Adenoma LGD	1
14	Polyp inside diverticulum	25	–	Sigmoid colon	EMR	Sessile serrated adenoma[a]	1
15	Size and location	50	Adenoma LGD	Caecum and ascending colon	EMR + stapling	Adenoma HGD	1
16	Size and location	50	Adenoma LGD	Hepatic flexure	EMR	Adenoma HGD	1
17	Anatomical location	10	–	Appendiceal orifice	Stapling	Adenoma LGD	1
18	Size and location	50	Adenoma LGD	Ascending colon	EMR	Adenoma LGD	1
19	Non-lifting polyp	30	Adenoma LGD	Ascending colon	Stapling	Adenoma HGD	1
20	Size and location	40	Adenoma LGD	Adjacent to the ileocecal valve	Lap. surgery	Adenoma HGD	4
21	Non-lifting polyp	35	Adenoma HGD	Hepatic flexure	Stapling	Adenoma LGD + schwannoma	16
22	Anatomical location	25	–	Appendiceal orifice	Stapling	Adenoma LGD	1
23	Non-lifting polyp	15	Adenoma LGD	Ascending colon	Lap. surgery	Adenocarcinoma, pT3N0M0	12
24	Anatomical location	30	–	Appendiceal orifice	Stapling	Adenoma LGD	1
25	Non-lifting polyp	15	Adenoma LGD	Caecum	Stapling	Adenoma LGD	0

CELS = combined endoscopic and laparoscopic surgery; EMR = endoscopic mucosal resection; HGD = high-grade dysplasia; Lap. = laparoscopic; LGD = low-grade dysplasia; LOS = length of stay.
a) With dysplasia.

ity, surgical resection was not attempted. Histopathology showed adenoma with low-grade dysplasia and the patient is now under endoscopic surveillance.

In patient no. 20, the lesion was circumferential and located in the terminal ileum, which was not obvious during the primary colonoscopy. Therefore, the CELS was not performed but instead continued as laparoscopic segmental surgery, also to avoid stenosis.

Procedure-related complications during the first 30 post-operative days were observed in four patients. Two patients (no. 4 and 22) developed a subcutaneous haematoma at one of the port sites and were treated conservatively. One patient (no. 21) was suspected of a micro-perforation in the sigmoid colon after an endoscopically assisted laparoscopic resection at the hepatic flexure. During colonoscopy at the CELS procedure, a benign stricture and diverticula were noted in the sigmoid colon, but no signs of perforation were present during or after the procedure. An abdominal CT was performed on post-operative day seven. demonstrating a small extra-colonic fluid collection with small air bubbles. As the patient revealed no signs of peritonitis or sepsis, she was treated with intravenous antibiotics and was discharged from hospital on day 16. Patient no. 23, who was treated with a right hemicolectomy, developed abdominal pain and fever on post-operative day seven. Diagnostic laparoscopy was performed without any intra-abdominal pathology. The patient was treated conservatively and stayed hospitalised for 12 days.

DISCUSSION

The aim of our study was to investigate whether CELS is a feasible alternative to colonic resection in patients with benign but endoscopically unresectable lesions. We also chose to offer endoscopically assisted CELS to severely co-morbid patients with small malignant lesions without signs of locally or systemically advanced disease. Our results show that the procedures are feasible with reasonable procedure times, rates of complication and length of stay.

Previous studies also strongly indicate that CELS is an effective and safe method to avoid segmental colectomy, with success rates ranging from 73% to 88% and complication rates from 9% to 13% [3, 6, 7]. In their randomised controlled trial with laparoscopic right colectomy versus CELS, Lascarides et al showed that patients undergoing CELS had a significantly shorter time to pass flatus, resumed a solid diet and had a shorter length of hospital stay. There was no difference in complication rates [4].

CELS procedures are dynamic processes in the sense that, although surgeons decide on one surgical technique prior to surgery, it may be changed as the procedure progresses. For instance, a laparoscopically assisted endoscopic mucosal resection may be attempted, but if full resection turns out to be unattainable, the team may choose to remove the lesion by stapling it off. If, during the resection, it becomes evident that the lesion is malignant, and the patient is in otherwise good health, the operating team may choose to proceed to full oncological resection immediately. Therefore, it is important that the operating teams include both skilled laparoscopic colorectal surgeons and expert endoscopists. Conversion to colonic resection should not be characterised as a failure, and our results clearly demonstrate that in all three cases, the perioperative decision to perform resection rather than continuing with EMR or laparoscopic stapling was correct.

Patients with endoscopically unresectable benign lesions are treated with segmental colon resection, with the risk of post-operative complication and hospitalisation. Due to reduced surgical trauma, the CELS procedure will result in a reduced number of colon resections in patients with benign lesions. Recent evidence shows that one in five patients have bowel dysfunction affecting their quality of life several years after colon resections [8]. This minimally invasive procedure may yield a better long-term quality of life.

Patients who were offered a CELS procedure were evaluated at an MDT conference. By default, we have MDT conferences to evaluate all malignant colonic lesions. This manner of dealing with malignant colonic lesions stems from a demand from the Danish Health authorities [9] based on international recommendations [10]. We have thus expanded this procedure to apply to benign colon lesions that are unsuitable for standard endoscopic treatment.

The present study has some limitations. The low number of patients affects the applicability of the results in clinical practice, particularly since CELS is used in frail co-morbid patients with known adenocarcinoma. Also, this was a retrospective study with selected patients; however, it is a consecutive case series, which adds to existing knowledge of CELS. Our results are compelling and with the increasing incidence of benign lesions and early cancer due to the colorectal cancer screening programmes, CELS is an alternative path for minimally invasive removal of colonic lesions. This may improve patient outcome and cost-effectiveness, but a prospective randomised controlled trial is needed to evaluate the outcome, morbidity and oncological effect.

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