A multicentre, prospective, observational cohort study of variation in practice in perioperative analgesia strategies in elective laparoscopic colorectal surgery (the LapCoGestic study)

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ABSTRACT

INTRODUCTION Enhanced recovery programmes are established as an essential part of laparoscopic colorectal surgery. Optimal pain management is central to the success of an enhanced recovery programme and is acknowledged to be an important patient reported outcome measure. A variety of analgesia strategies are employed in elective laparoscopic colorectal surgery ranging from patient-controlled analgesia to local anaesthetic wound infiltration catheters. However, there is little evidence regarding the optimal analgesia strategy in this cohort of patients. The LapCoGestic study aimed to explore differences in analgesia strategies employed for patients undergoing elective laparoscopic colorectal surgery and to assess whether this variation in practice has an impact on patient-reported and clinical outcomes.

MATERIALS AND METHODS A prospective, multicentre, observational cohort study of consecutive patients undergoing elective laparoscopic colorectal resection was undertaken over a two-month period. The primary outcome measure was postoperative pain scores at 24 hours. Data analysis was conducted using SPSS version 22.

RESULTS A total of 103 patients undergoing elective laparoscopic colorectal surgery were included in the study. Thoracic epidural was used in 4 (3.9%) patients, spinal diamorphine in 56 (54.4%) patients and patient-controlled analgesia in 77 (74.8%) patients. The use of thoracic epidural and spinal diamorphine were associated with lower pain scores on day 1 postoperatively ($P < 0.05$). The use of patient-controlled analgesia was associated with significantly higher postoperative pain scores and pain severity.

DISCUSSION Postoperative pain is managed in a variable manner in patients undergoing elective colorectal surgery, which has an impact on patient reported outcomes of pain scores and pain severity.

KEYWORDS

Analgesia – Laparoscopy – Colorectal surgery

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Introduction

The use of standardised enhanced recovery programmes in combination with laparoscopic surgery has revolutionised clinical and patient-reported outcomes in elective

colorectal surgery. Central to the success of enhanced recovery programmes is optimal pain management. Optimal pain relief is reported to be one of the most important outcome measures for patients undergoing surgery.^{1,2}

However, despite this, it is estimated that approximately 40% of patients experience severe postoperative pain.^{2,3}

The surgical stress response is attenuated in elective laparoscopic surgery,^{4–6} which clinically translates into reduced postoperative pain, earlier return of gastrointestinal function and reduced length of hospital stay.^{7–15} Alongside the use of enhanced recovery programmes, one of the key elements to minimising the surgical stress response is an appropriate analgesic regimen.^{14,15} The ideal analgesic regimen in elective laparoscopic surgery should ensure adequate pain relief, enable early mobilisation and the early return of gastrointestinal function combined with a low adverse effect profile. A number of analgesia strategies are available to be employed in laparoscopic colorectal surgery, including, thoracic epidural, spinal analgesia, patient-controlled analgesia, subcutaneous and/or intraperitoneal local anaesthetics, local anaesthetic wound infiltration catheters and transverse abdominal plane blocks. However, there is a paucity of data identifying the ideal analgesic regimen in laparoscopic colorectal surgery. Consequently, there remains a lack of consensus on the optimal perioperative analgesia strategy in this cohort of patients,^{16,17} thus leading to colorectal units employing analgesic regimens based on individual expertise and experience.

The aim of this exploratory study was to identify the variation in analgesia strategies in patients undergoing elective laparoscopic colorectal surgery. The North East of England is well placed to conduct this study given its consistency in having the highest rates of laparoscopic colorectal surgery in the UK according to the National Bowel Cancer Audit reports.¹⁸

Materials and methods

The LapCoGestic study was a prospective, multicentre, observational cohort study. It was conducted over a two-month period across twelve NHS hospitals in the North East of England.¹⁹ Members of the trainee collaborative identified consecutive patients undergoing laparoscopic elective colorectal resections. Study inclusion criteria included all adult patients (over 18 years old) undergoing an elective laparoscopic (multi- or single-port) colorectal resection. Exclusions included patients undergoing emergency surgery, a diagnostic laparoscopy, or with a pre-existing chronic pain or fatigue syndromes, chronic opioid use or cognitive impairment.

The primary outcome measure was postoperative pain scores at 24 hours. This is the recommended outcome measure by the Royal College of Anaesthetists to assess the efficacy of postoperative analgesia.²⁰ Pain scores were collected using a validated numerical rating 10-point scale. Clinically significant differences between differing analgesia strategies were determined when there was a difference of 1.3 U on a numerical rating scale of 0–10.^{21,22} Pain severity was defined as ‘no pain’ if 0 was scored, ‘mild pain’ for scores of 1–3, ‘moderate pain’ for scores of 4–6 and ‘severe pain’ for scores of 7–10. Secondary outcome measures were postoperative opioid analgesic use, total

length of stay, 30-day postoperative complication rates, complication grade according to the Clavien–Dindo classification and 30-day reoperation and readmission rates.

The National Research Ethics Service provided ethical review. Local approval was sought from all participating centres. This manuscript has been reported in accordance with the Strengthening the Reporting of Cohort Studies in Surgery statement.²³

Data collection and management

A standardised data collection spreadsheet (Microsoft Excel 2010) was used at each centre with predefined data fields. Following completion of the study, all anonymised data were submitted centrally via a secure, password protected website. All anonymised data were subsequently analysed.

Statistical analysis

The results of this study were prepared in accordance to guidelines set by the Strengthening the Reporting of Observational Studies in Epidemiology statement.²⁴ Basic descriptive statistics were used to denote pain scores. Data were collected and analysed in clinically relevant categories. The independent student t-test was used to examine differences in mean scores in two groups and the one-way analysis of variance (ANOVA) for more than two groups. Excel 2010 was used for data handling, and statistical modelling was performed in SPSS version 22. Statistical significance is defined as a *P*-value of 0.05 or less in all analyses.

Results

A total of 103 patients underwent an elective laparoscopic colorectal resection during the study period, of whom 60 (58.3%) were male, with a median age of 66 years. Colorectal malignancy was the most common indication for operative intervention, with 76 (73.8%) colonic resections undertaken. The total conversion rate was 13.6% with 14 conversions to open surgery. Patient and clinical demographics are highlighted in Table 1.

Intraoperative analgesic regimen

All patients had a multimodal intraoperative analgesic regimen comprising simple analgesics and opioid-based analgesia (Table 2). Thoracic epidural was the least commonly used analgesic agent in patients undergoing an elective colorectal resection, with this analgesia strategy employed in four patients (3.9%). Non-steroidal anti-inflammatory drugs were only used in nine patients (8.7%). Regional nerve blocks were used in 30 patients (29.1%), of whom 11 patients (10.7%) received a rectus sheath catheter with continuous infusion and 19 (18.4%) received a transversus abdominus plane block. The most common opioid-based analgesic agent was spinal diamorphine, with this being the primary intraoperative analgesia strategy in 54.4% of patients. There was considerable variation in the dose of spinal diamorphine used across the region, with a median dose of 500 mg (interquartile range, IQR, 500–1500 mg) being administered.

Postoperative analgesic regimen

Most patients received a multimodal postoperative analgesic regimen. Opioid-based patient-controlled analgesia was the most commonly used postoperative opioid analgesic agent, with 74.8% of patients receiving this treatment immediately postoperatively (Table 2). No patients received 'rescue' patient-controlled analgesia because of severe pain. Of the 14 patients who underwent conversion,

all patients received patient-controlled analgesia, with 5 patients (35.7%) also receiving rectus sheath catheters.

Thoracic epidural was the least commonly employed analgesia strategy, with only 1.9% of patients receiving this type of analgesia. Other modalities of postoperative analgesia included transversus abdominus plane blocks with continuous local anaesthesia infusion (11.7%), nefopam (30.1%), codeine phosphate (6.8%), tramadol (18.4%) and morphine sulfate (Oromorph®; 24.3%; Table 2).

Postoperative pain scores

The use of spinal diamorphine and intravenous morphine was associated with clinically and statistically significant lower pain scores on postoperative day 1 (Table 3). On converting pain scores to correlate with pain severity, the relationship between the use of spinal diamorphine and lower pain severity was preserved, with fewer episodes of moderate and severe pain reported on postoperative day 1 ($P = 0.02$) (Table 3). Patients receiving intraoperative spinal diamorphine received lower doses of postoperative

Table 1 Patient and clinical demographics.

Variable	Patients, n (%)
Median age (years)	66
Sex:	
Male	60 (58.3)
Female	43 (41.7)
Body mass index (kg/m ²):	
18–24.9	38 (36.9)
25–29.9	37 (35.9)
30–34.9	17 (16.5)
35–39.9	7 (6.8)
> 40	4 (3.9)
American Society of Anesthesiologists score:	
I	8 (7.8)
II	66 (64.1)
III	28 (27.2)
IV	1 (1.0)
Operative indication:	
Ulcerative colitis	8 (7.8)
Colorectal malignancy	76 (73.8)
Crohn's disease	9 (8.7)
Diverticular disease	3 (2.9)
Other	7 (6.8)
Surgery:	
Subtotal colectomy	6 (5.8)
Restorative proctectomy and ileoanal pouch	3 (2.9)
Completion proctectomy	7 (6.8)
Panproctocolectomy	2 (1.9)
Anterior resection ± ileostomy	35 (34.0)
Right hemicolectomy	31 (30.9)
Sigmoid colectomy	3 (2.9)
Hartmann's procedure	7 (6.8)
Abdominoperineal resection of rectum	6 (5.8)
Left hemicolectomy	2 (1.9)
Transverse colectomy	1 (1.0)

Table 2 Intra- and postoperative analgesia regimens.

Analgesia	Patients, n (%)	
	Yes (%)	No (%)
Intraoperative:		
Paracetamol	73 (70.9)	30 (29.1)
NSAIDs	9 (8.7)	94 (91.3)
Fentanyl	32 (31.1)	71 (68.9)
Alfentanil	4 (3.9)	99 (96.1)
Remifentanyl	40 (38.8)	63 (61.2)
Morphine	45 (43.7)	58 (56.3)
Spinal diamorphine	56 (54.4)	47 (45.6)
Epidural	4 (3.9)	99 (96.1)
Regional nerve blocks	30 (29.1)	73 (70.9)
Local anaesthesia	42 (40.8)	61 (59.2)
Postoperative:		
Paracetamol	102 (99.0)	1 (1.0)
Patient-controlled analgesia	77 (74.8)	26 (25.2)
Transversus abdominus plane blocks ^a	12 (11.7)	91 (88.3)
Nefopam	31 (30.1)	72 (69.9)
Codeine phosphate	7 (6.8)	96 (93.2)
Tramadol	19 (18.4)	84 (81.6)
Morphine sulfate (Oromorph®)	25 (24.3)	78 (75.7)
Epidural	2 (1.9)	101 (98.1)

^a Rectus sheath catheters with continuous local anaesthetic infusion

opioid analgesia on day 1; however, this failed to achieve statistical significance (29.5 mg vs 41.5 mg respectively, $P = 0.07$; Table 3).

In patients who underwent conversion, mean postoperative day 1 pain scores were 2.28 compared with 2.64 ($P = 0.57$) in the laparoscopic group. Mean opioid use was higher in the converted group compared with the laparoscopic group, 44 mg and 33.18 mg, respectively ($P = 0.03$).

Patients receiving a patient-controlled analgesia had clinically and statistically significantly higher pain scores on postoperative day 1 (patient-controlled analgesia 3.01 vs no patient-controlled analgesia 1.83; $P = 0.03$) (Table 5).

The use of PCA was associated with a higher number of moderate and severe episodes of pain than in the no patient-controlled analgesia group, $P = 0.02$ (Table 4). Significantly higher rates of postoperative opioid analgesia use were associated with the use of patient-controlled analgesia in the first 24 hours postoperatively (Table 4). Patients receiving an epidural had clinically and statistically significantly lower pain scores in the first 48 hours postoperatively ($P < 0.05$; Fig 1). On measuring postoperative pain scores over a seven-day period, there was no single analgesic agent that demonstrated consistent superior outcomes in terms of pain scores, pain severity and opioid use (Fig 1).

Table 3 Intraoperative analgesic regimen and pain-related outcomes.

Drug	Postoperative pain						Day 1 opioid use		
	(n)	Score	P-value	Mild	Severity		P-value	Mean (mg)	P-value
		(mean)			Moderate	Severe			
Paracetamol:									
Yes	71	2.68	0.74	19	21	6	0.54	36	0.61
No	28	2.86		9	11	1		32.24	
NSAIDs:									
Yes	8	2.62	0.90	3	2	1	0.82	33.92	0.92
No	91	2.74		25	30	6		35.02	
Fentanyl:									
Yes	69	2.73	0.98	12	11	1	0.15	35.74	0.71
No	30	2.73		16	21	6		33.06	
Alfentanil:									
Yes	4	3.00	0.72	2	2	0	0.43	32	0.86
No	95	2.72		26	30	7		35.05	
Remifentanyl:									
Yes	37	2.73	0.99	11	14	1	0.50	36.27	0.75
No	62	2.73		17	18	6		34.06	
Morphine:									
Yes	43	2.20	0.01	11	17	5	0.13	36.73	0.63
No	56	3.42		17	15	2		33.51	
Spinal diamorphine:									
Yes	55	2.18	0.01	16	14	3	0.02	29.55	0.07
No	44	3.41		12	18	4		41.47	
TAP blocks:									
Yes	29	2.86	0.72	6	9	3	0.59	34.72	0.96
No	70	2.67		22	23	4		35.02	
Local anaesthesia:									
Yes	40	2.83	0.74	10	14	3	0.93	35.21	0.94
No	59	2.66		18	18	4		34.74	
NSAIDS, non-steroidal anti-inflammatory drugs; TAP, transversus abdominus plane.									

NSAIDS, non-steroidal anti-inflammatory drugs; TAP, transversus abdominus plane.

Table 4 Postoperative analgesic regimen and pain-related outcomes.

Drug	Postoperative pain						Day 1 opioid use		
	Score			Severity			P-value	Mean (mg)	P-value
	(n)	(mean)	P-value	Mild	Moderate	Severe			
Paracetamol:									
Yes	98	2.72	0.91	27	32	7	0.45	–	–
No	1	3		1	0	0			
Morphine PCA:									
Yes	75	3.01	0.03	25	24	7	0.02	39.29	0.02
No	24	1.83		3	8	0		21.48	
TAP blocks:									
Yes	12	2.25	0.48	3	4	0	0.70	25.42	0.30
No	87	2.79		25	28	7		36.2	
Nefopam:									
Yes	29	2.66	0.85	5	12	1	0.26	35.55	0.90
No	70	2.76		23	20	6		34.66	
Codeine phosphate:									
Yes	7	4.14	0.21	2	2	2	0.12	22.14	0.30
No	92	2.62		26	30	5		35.87	
Tramadol:									
Yes	18	2.89	0.78	4	8	1	0.68	45.54	0.17
No	81	2.69		24	24	6		32.5	
Morphine sulfate (Oromorph®):									
Yes	24	2.38	0.38	7	9	0	0.47	34.81	0.98
No	75	2.84		21	23	7		34.97	
Epidural:									
Yes	4	0.50	0.01	1	0	0	0.26	34.75	0.992
No	95	2.82		27	32	7		34.94	
PCA, patient-controlled anaesthesia; TAP, transversus abdominus plane.									

PCA, patient-controlled anaesthesia; TAP, transversus abdominus plane.

Postoperative outcomes

The overall median length of hospital stay was six days (IQR 4–8 days; Table 5). Thirty patients (29.1%) required a postoperative high-dependency unit stay. Thirty-day morbidity was 38.8%, with grade II Clavien–Dindo complications being the most common. A total of 55 complications were documented in 40 patients. Severe complications, Clavien–Dindo classification greater than III occurred in 5.8% of patients. Thirty-day reoperative rate was 2.9%, with three patients returning to theatre for bleeding, drainage of a pelvic collection and revision of a stoma.

Discussion

This study demonstrates the wide variation in the perioperative analgesia strategy employed for patients undergoing

elective colorectal surgery in the North East of England. Previous studies have documented the lack of consensus in the optimal analgesia strategy in laparoscopic colorectal surgery and the consequent variation in elective practice.^{25,26} However, these studies have surveyed the practice of clinicians, primarily, anaesthetists, with regards to their preferred mode of analgesia within the elective laparoscopic colorectal setting. This study is unique in that it prospectively examines regional practice in analgesia strategies and correlates this with patient-reported outcomes of pain and pain severity.

This study clearly demonstrates significant variation in clinical practice, with intraoperative spinal diamorphine and postoperative patient-controlled analgesia being the most common analgesia strategies employed. We have identified intraoperative spinal diamorphine to be associated with clinically and statistically lower pain scores and pain severity at 24 hours postoperatively and patient-

Table 5 Postoperative outcomes.

Variable	Frequency, n (%)
Median length of stay	6 (IQR 4-8)
30-day morbidity rate	40 (38.8)
30-day reoperative rate	3 (2.9)
30-day readmission rate	13 (12.6)
30-day mortality	0 (0.0)
Complications:	
Electrolyte abnormality	4 (3.9)
Arrhythmia	2 (2.0)
Urinary retention	1 (1.0)
High output stoma	1 (1.0)
Anastomotic leak	2 (2.0)
Wound Infection	12 (11.6)
Intra-abdominal collection	5 (4.8)
Pneumonia	4 (3.9)
Gastrointestinal haemorrhage	4 (3.9)
Acute kidney injury	2 (2.0)
Paralytic ileus	12 (11.6)

controlled analgesia to be associated with higher postoperative pain scores and pain severity. Despite these results, we have failed to identify a single or combination of analgesic agents that provide consistently good analgesia within the postoperative period.

Analgesia strategies in elective laparoscopic colorectal surgery are often complex and, as demonstrated by our study, are multimodal. Appropriate consideration is required in selecting the optimal, multimodal analgesia regimen, as different analgesic agents may provide optimal pain relief at different postoperative time points. Current guidelines on perioperative analgesia strategies in elective laparoscopic colorectal surgery fail to give explicit guidance on the optimal regimen to employ in this cohort of patients, and base their recommendations on evidence of low to moderate quality.¹⁶ This lack of guidance naturally translates into clinical variation. The multimodal nature of perioperative analgesia is yet to be examined robustly in elective laparoscopic colorectal surgery. Limited work on employing a multimodal analgesic approach compared with epidural alone in open colorectal surgery reported equivalent pain scores between the two arms, but a shorter length of critical care and overall hospital stay in the multimodal arm.²⁷ Similar work is required in laparoscopic colorectal surgery to determine which combination of analgesic agents is associated with the best clinical and patient-reported outcomes in the perioperative period.

Our experience with limited use of epidural analgesia in elective laparoscopic colorectal practice is reflective of an evolving analgesia strategy in this cohort of patients. A

nationwide analysis of elective colorectal practice in the United States using the national inpatient sample database revealed a similarly low rate of epidural use of 2.14%.²⁸ There has been a steady movement away from the use of epidural analgesia in recent times, with a trend towards the use of patient-controlled analgesia and spinal diamorphine in elective laparoscopic colorectal surgery.²⁶ This follows reports from a number of randomised controlled trials reporting prolonged postoperative recovery with epidural use, including increased length of hospital stay, delayed return to bowel function and higher risk of postoperative ileus.^{29,30} Despite these potential limitations, the analgesic quality of the thoracic epidural is well regarded, especially when compared with patient-controlled analgesia use.^{31,32} Our study correlates with these trials in terms of reporting higher pain scores and more episodes of severe pain with patient-controlled analgesia use, in comparison with other analgesic modalities including epidural and spinal diamorphine. A 2015 retrospective cohort study demonstrated equivalence in key clinical outcomes including pain scores, length of stay and morbidity between patients receiving patient-controlled analgesia and those not receiving patient-controlled analgesia in patients undergoing laparoscopic colorectal surgery, suggesting that alternative analgesia strategies may be of similar value in this cohort of patients.³³

Our study identifies a number of analgesic agents that are efficacious in reducing postoperative pain in patients undergoing elective laparoscopic colorectal surgery, by attributing a numerical value to postoperative pain and pain severity. However, modest reductions in pain scores do not necessarily equate to clinically meaningful outcomes. Pain scores represent one facet of postoperative patient-reported outcomes and need to be appropriately correlated with other measures of patient-centric outcomes including quality of life and quality of recovery.

The aim of this exploratory study was to generate hypotheses for future work. It is clearly demonstrated that there is significant variation in clinical practice, which has an impact on patient reported outcomes of pain. However, it is difficult to ascertain the optimal multimodal analgesia strategy based on our results, owing to the limited sample size of our study and the potential crossover among analgesia regimens. Further work is required to look at the best combination of intra- and postoperative analgesia in patients undergoing elective laparoscopic colorectal surgery within a more robust study design to help inform and guide clinical practice. Key future works will include exploring patient and clinician equipoise with regards to designing optimal analgesia strategies which can be tested prospectively in future clinical trials, identifying optimal clinical and patient reported endpoints and assessing the feasibility of delivering such a trial.

Conclusion

Our study documents the wide variation in the analgesia regimens employed in the elective laparoscopic colorectal

setting and correlates this variation with important outcomes related to pain, including pain scores, severity and the need for opioid analgesia.

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