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2 **Randomized clinical trial on Epidural *versus* Patient-controlled Analgesia for**
3 **laparoscopic colorectal surgery within an enhanced recovery pathway**

4
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17
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19 Key words: Epidural, colorectal surgery, laparoscopy, enhanced recovery.

20 Abbreviations: EDA – epidural analgesia, PCA – patient-controlled analgesia,
21 ERAS[®] - enhanced recovery after surgery.

22 Statistics Abstract 250 words, Manuscript 2876 words, 5 inserts (1 Table, 4
23 Figures), references 33, Online material.

24
25 Running title: Epidurals for laparoscopic colorectal surgery

26 **Miniabstract**

27 128 patients undergoing elective laparoscopic colorectal resections were randomized
28 to epidural (EDA) *versus* patient-controlled opioid-based analgesia (PCA). Medical
29 recovery and high dependency stay were longer in EDA patients but hospital stay
30 was similar. 30% of EDA patients needed transitory vasopressor treatment. There
31 was no difference in postoperative pain scores.

32 **Abstract**

33 **Objective:** To compare epidural analgesia (EDA) to patient-controlled opioid-based
34 analgesia (PCA) in patients undergoing laparoscopic colorectal surgery.

35 **Summary background data:** EDA is mainstay of multimodal pain management
36 within enhanced recovery pathways (ERAS[®]). For laparoscopic colorectal resections,
37 the benefit of epidurals remains debated. Some consider EDA as useful, while others
38 perceive epidurals as unnecessary or even deleterious.

39 **Methods:** A total of 128 patients undergoing elective laparoscopic colorectal
40 resections were enrolled in a randomized clinical trial comparing EDA *versus* PCA.
41 Primary endpoint was medical recovery. Overall complications, hospital stay,
42 perioperative vasopressor requirements, and postoperative pain scores were
43 secondary outcome measures. Analysis was performed according to the intention-to-
44 treat principle.

45 **Results:** Final analysis included 65 EDA patients and 57 PCA patients. Both groups
46 were similar regarding baseline characteristics. Medical recovery required a median
47 of 5 days (IQR 3;7.5) in patients with EDA and 4 days (IQR 3;6) in the PCA group
48 ($P= 0.082$). PCA patients had significantly less overall complications (19 (33%) vs. 35
49 (54%); $P= 0.029$) but a similar hospital stay (5 days (IQR 4;8) vs. 7 days (IQR
50 4.5;12); $P= 0.434$). Significantly more EDA patients needed vasopressor treatment
51 perioperatively (90 vs. 74%, $P= 0.018$), the day of surgery (27 vs. 4%, $P< 0.001$), and
52 on postoperative day 1 (29 vs. 4%, $P< 0.001$), while no difference in postoperative
53 pain scores was noted.

54 **Conclusions:** Epidurals appear to slow down recovery after laparoscopic colorectal
55 resections without adding obvious benefits. EDA can therefore not be recommended
56 as part of ERAS[®] pathways in laparoscopic colorectal surgery.

57 **Registration number: NCT00508300 (<http://www.clinicaltrials.gov>).**

58 Introduction

59 Enhanced recovery (ERAS[®]) pathways have proven to reduce significantly
60 complications, postoperative length of stay and costs after colorectal surgery¹⁻³. The
61 multimodal treatment bundle contains about 20 individual items to attenuate surgical
62 stress response and thus to improve recovery^{4, 5}. High compliance with the
63 recommended pathway was strongly correlated with favorable clinical outcomes⁶.
64 Previous randomized trials identified optimized fluid management, minimal invasive
65 surgery, and epidural analgesia (EDA) as key items of ERAS[®] concepts^{2, 7}.

66 The benefit of EDA however remains controversial especially when combined
67 with minimal invasive surgery⁸⁻¹². Expert laparoscopic centers have reported
68 excellent outcomes without use of EDA¹³⁻¹⁶. Moreover, a recent prospective study
69 suggested even slower recovery if EDA was employed after laparoscopic
70 colectomy¹⁶. Furthermore, novel strategies for pain management rendered promising
71 results^{17, 18}. This obvious mismatch of recommendations, available evidence and
72 current practice can only be reconciled with more prospective data.

73

74 The aim of this prospective randomized trial was therefore to test the
75 hypothesis that EDA improves recovery after laparoscopic colorectal resections when
76 compared with patient-controlled opioid-based analgesia (PCA).

77

78 **Methods**

79 *Study design*

80 A single center, prospective parallel-group superiority study with balanced
81 randomization (1:1) was performed to compare the clinical effects of EDA vs.
82 morphine-based PCA (EvA trial) in patients undergoing laparoscopic colorectal
83 resections.

84 The institutional ethics committee approved the study (# 166/07), and all
85 patients provided written informed consent before enrollment. The trial was
86 registered under clinicaltrial.gov (trial # NCT00508300) before patient recruitment
87 was started.

88

89 *Patients and setting*

90 All patients undergoing elective laparoscopic colorectal surgery at the
91 University Hospital of Lausanne (CHUV), a tertiary referral center in Switzerland,
92 were assessed for eligibility. Exclusion criteria included age below 18 years, inability
93 to provide informed consent, and medical contraindication for EDA according to
94 institutional guidelines^{19, 20}.

95

96 *Enrolment and randomization*

97 Patients were assessed for eligibility at outpatient consultation by the
98 operating surgeon once the indication for surgery was established. Patients received
99 oral and written information on the study before written consent was obtained.

100 Patients were randomly assigned by a dedicated study nurse using an online
101 randomization program (Randomizer, Institute for Medical Informatics, Statistics and
102 Documentation, Medical University of Graz, Austria; URL: <http://www.randomizer.at>).

103 For medical and logistic reasons, blinding was not performed, as it appeared neither
104 feasible nor realistic for this present study.

105

106 *Interventions, anesthesia and pain strategy*

107 Patients were randomized the day prior to surgery to allow for appropriate
108 information on the anesthesia technique.

109 In the EDA group, epidural catheter was inserted at thoracic level (Th 8-10)
110 before induction of anesthesia. A bolus of 5ml of bupivacaine 0.5% was started as
111 soon as the epidural catheter was in place, and a continuous perfusion of
112 bupivacaine 0.5% at 5 ml/h was initiated until the end of surgical procedure.

113 In both groups, induction of anesthesia was performed with propofol 1-2
114 mg/kg, fentanyl 2-3 µg/kg and cisatracurium (0.15-0.2 mg/kg) for muscle paralysis.
115 After tracheal intubation, maintenance of anesthesia was performed with sevoflurane
116 in a mixed oxygen/air fresh gaz, and cisatracurium as needed. Analgesia was
117 assured by the bupivacaine solution in the epidural group and by fentanyl as needed
118 in the PCA group.

119 At the end of surgery, a solution of bupivacaine 0.1%, fentanyl 2 µg/ml and
120 adrenaline 2 µg/ml was initiated in the epidural group at a rate of 6-10 ml/h (target:
121 VAS<4) with bolus of 3 ml of the solution allowed every 40 minutes (Patient
122 Controlled Epidural Analgesia)²⁰. In the PCA group, iv PCA with morphine 1 mg/ml,
123 with bolus of 1 ml at every 5 minutes and a locked of 40 mg/4 hours was inserted.
124 All patients received paracetamol 4x1g/day and metamizole 4x500mg/day as
125 baseline analgesic treatment unless contraindicated. Pain assessment was done
126 twice daily at rest and on mobilization or coughing by a dedicated institutional
127 analgesia team. Failure of either technique (VAS persistently >3) was recorded by
128 the analgesia team and rescue pain relief was administered if necessary (morphine

129 subcutaneously 0.1 mg/kg maximum 6x/d or buprenorphine sublingual 0.2-0.4 mg
130 maximum 3x/d). Both interventions were planned to be discontinued on postoperative
131 day (POD) 2 following international recommendations^{21, 22}. EDA and PCA could be
132 continued if the analgesia team judged that a prolonged application was beneficial for
133 the patient. The day of discontinuation was documented.

134 During anesthesia and for the following postoperative days, maintenance of
135 blood pressure >60mmHg or diuresis > 0.5 ml/kg/h was aimed for, first by
136 administration of volume, Ringer-lactate 500 ml or 500 ml colloids (Voluven®).
137 Noradrenaline at a dose of 0-10µg/h was used as vasopressor if blood pressure was
138 not corrected by volume administration. Substitution of blood products was done if
139 hematocrit < 25%, or at the discretion of the anesthetist in charge of the procedure.

140

141 *Perioperative care pathway*

142 Enhanced recovery was introduced in our institution in 2006 using a protocol
143 which was adapted after a first randomized trial from our group². After the recruitment
144 for the present EvA trial had started, it was decided in June 2011 to adapt the
145 pathway according to the in meantime published ERAS® recommendations²¹ and to
146 reinforce application of the pathway by a structured implementation program. Our
147 ERAS® pathway complies with the most recent ERAS® guidelines^{4, 5} and was
148 reported along with clinical and economic outcomes in 2013³.

149

150 *Outcomes/study endpoints*

151 Outcomes were analyzed according to the intention-to-treat principle. Medical
152 recovery was chosen as primary endpoint and was defined as meeting *all* of the
153 three following criteria: (I) sufficient *pain control* by oral analgesics, (II) *fully mobilized*
154 or at least comparable with preoperative status, and (III) tolerance of oral food which

155 was defined as $\geq 2/3$ of normal meal (hospital portion)²³. Medical recovery was
156 considered as more specific outcome parameter than hospital stay, as social and
157 logistic factors are not interfering^{24, 25}. Secondary endpoints were postoperative
158 hospital stay and length of stay in the high dependency unit. Postoperative 30-day
159 morbidity was graded by use of the Dindo-Clavien classification²⁶; major
160 complications were defined as complication grade 3-5. Use of perioperative
161 vasopressor treatment was documented for every patient until 4 days after surgery.
162 Pain relief was assessed by use of a visual analogue scale (VAS: 0-10) with a
163 baseline value the day before surgery; routine evaluation twice daily started the
164 evening of the surgery day and was continued until POD 4.

165 Demographic information (age, gender, body mass index, Charlson co-
166 morbidity index²⁷, and the American Society of Anesthesiologists (ASA) grade) as
167 well as pertinent surgical information (indication, type of surgery, conversion rate,
168 operation time, estimated blood loss) were all predefined. Outcomes were assessed
169 by dedicated study nurses who entered data in a specifically designed computerized
170 database.

171

172 *Subgroup analyses*

173 EDA group happened to have more overall and major complications that could
174 not be attributed to the allocated analgesic interventions as suggested by previous
175 studies^{1, 8}. Major complications prolong medical recovery and hospital stay and entail
176 thus an obvious bias in favor of the PCA group²⁸. For this reason, a *post hoc*
177 subgroup analysis excluding patients with major complications was additionally
178 performed.

179 Primary and secondary endpoints depend not only on the allocated analgesic
180 intervention but also heavily on the global perioperative care strategy^{3, 6, 15, 25}. With

181 the adaptation of the institutional enhanced recovery pathway to ERAS[®] guidelines
182 during the study period, it was decided to analyze patients within the full ERAS[®]
183 pathway separately as a subgroup.

184 The main purpose of these two additional analyses was to assess for potential
185 bias of those influencing factors in order to filter the intrinsic effect of EDA vs. PCA on
186 medical recovery and length of stay.

187

188 *Statistics*

189 Sample size computation based on a mean reduction of medical recovery time
190 of 1.5 ± 2.25 days by use of EDA^{2, 8, 29}. Adopting a power of 90%, a two-sided type I
191 error (α) of 0.05 and an anticipated drop-out rate of 10%, the calculated sample size
192 was 64 patients per group.

193 Descriptive statistics were reported as absolute or relative frequencies for
194 categorical variables and as median (range or interquartile range - IQR) or mean (\pm
195 SD) for continuous variables as appropriate. Fisher's exact test was employed to
196 analyze categorical variables. Student's *t* test and Mann-Whitney U test were used to
197 compare normal and non-normal continuous variables, respectively.

198 Data was analyzed by use of the Statistical Package for the Social Sciences
199 (SPSS 21.0, Inc., Chicago, IL USA) and Prism 6.03 (GraphPad[®] Software, Inc. 2236
200 Avenida de la Playa La Jolla, CA 92037 USA).

201 The trial was conducted and the results are presented according to the
202 CONSORT guidelines³⁰.

203 **Results**

204 Between February 10th 2010 and October 15th 2013, 266 consecutive patients
205 were assessed for eligibility. 138 patients did not meet the inclusion criteria or
206 refused to participate. The remaining 128 patients were randomized to receive either
207 EDA (n=67) or PCA (n=61) as allocated treatment. Two EDA patients and four PCA
208 patients dropped out after randomization and no patient was lost to follow-up. Final
209 analysis compared therefore 65 EDA patients with 57 patients with PCA (**Figure 1**).

210 Both comparative groups were similar in terms of pertinent demographic
211 parameters and surgical aspects as displayed in **Table 1**.

212

213 *Technical success rates and duration of EDA and PCA treatment*

214 Eight EDA were judged non-functioning and removed consistently on POD 0
215 (n=2) and POD 1 (n=6). Overall failure rate was thus 12%. EDA and PCA were
216 discontinued according to the study protocol on POD 2 in 47 (72%) and 55 (96%) of
217 patients, respectively ($P=0.005$). EDA was left in place in twelve of the remaining 18
218 patients until POD 3 and in 3 patients until POD 4. EDA was removed on POD 5, 6,
219 and 7 in one patient each. Treatment time was therefore significant longer in the EDA
220 group (2.33 ± 1.17 days vs. 1.65 ± 0.66 days, $P<0.001$). The urinary catheter was
221 removed on POD1 according to the protocol in 44 EDA patients (68%) and 28
222 patients (49%) of the PCA group ($P=0.044$). Urinary retention requiring reinsertion of
223 the Foley catheter occurred in 11 (17%) EDA and 7 (12%) PCA patients, respectively
224 ($P=0.611$).

225

226 *Medical recovery, complications and length of stay*

227 Medical recovery required a median of 5 (IQR 3;7.5) days in the EDA group
228 and 4 (IQR 3;6) days in patients with PCA ($P=0.082$). The 3 mandatory preconditions

229 for medical recovery were analyzed separately as well. *Full mobilization* and *oral pain*
230 *control* were achieved in both groups after a median of one and two days,
231 respectively. The last requirement met was *sufficient oral intake* after a median of 4
232 (IQR 2;6) days in EDA patients vs. 3 (IQR 2;4) days in the PCA group ($P=0.114$).
233 Median stay at the high dependency unit was 1 (IQR 1;2.5) day vs. 1 (IQR 0;1) day
234 for EDA and PCA group, respectively ($P=0.213$).

235 Thirty-five out of 65 EDA patients and 19 of 57 PCA patients developed
236 postoperative complications ($P=0.029$). The detailed grading of severity and a list of
237 individual complications are provided as **online appendix (A, B)**.

238 Hospital stay was 7 (IQR 4.5;12) days for patients with EDA and 5 (IQR 4;8) days in
239 the PCA group ($P=0.434$). Three patients from the EDA group were readmitted after
240 discharge (PCA: 0; $P=0.247$).

241

242 *Perioperative fluid management, vasopressor requirements and perioperative pain*

243 Perioperative fluid management was similar between the groups. EDA and
244 PCA patients received 1604 ± 962 ml vs. 1575 ± 851 ml balanced crystalloids ($P=0.861$)
245 and 817 ± 429 ml vs. 664 ± 294 ml colloids ($P=0.051$). Weight gain on POD1 compared
246 to preoperatively was 1.45 ± 0.32 kg in the EDA group and 2.28 ± 0.56 kg in the PCA
247 group ($P=0.191$). Significantly more patients with EDA needed vasopressor treatment
248 during surgery and until POD 1, while no single patient required vasopressors after
249 POD 3 (**Figure 2**). Pain was overall well controlled by both modalities and no
250 significant differences were noted at any time point (**Figure 3**).

251

252 *Subgroup analysis*

253 A tendency to more major complications was observed in the EDA group (15
254 vs. 5, $P=0.213$). As major complications have a significant impact on primary and

255 secondary outcome measures, a *post hoc* analysis was performed excluding patients
256 with major complications. Fifty EDA patients were compared with 52 PCA patients.
257 Medical recovery and high dependency stay were significantly shorter in the PCA
258 group ($P=0.050$ and $P=0.010$), respectively, while hospital stay was similar (**Figure**
259 **4**). The ERAS[®] protocol was modified during the study period and the first 26
260 consecutive patients were not treated within the complete pathway as mentioned in
261 the methods section. The second subgroup analysis included therefore only patients
262 with full ERAS[®] pathway and having no major complication. Again, the PCA group
263 had significantly shorter medical recovery ($P=0.019$) and stay in the high dependency
264 unit ($P<0.001$) compared with patients having EDA (**online appendix C**).
265

266 Discussion

267 This present study shows that epidurals rather *impede recovery* after
268 laparoscopic colorectal resections without delivering superior pain relief or other
269 benefits. A major drawback identified was transitory hemodynamic instability
270 requiring vasopressor treatment in a significant proportion of EDA patients. So the
271 hypothesis was not verified and *enhanced recovery* pathways should not recommend
272 the use of epidurals for laparoscopic colorectal resections.

273

274 Main finding of the present study was a trend for longer medical recovery in
275 EDA patients that became significant in the analyzed subgroups. One explanation
276 might be the transitory hemodynamic instability due to sympathetic blockage in
277 patients with EDA as confirmed by our reports and by others^{8, 31, 32}. This also explains
278 the observed longer stay in the high dependency unit. Overall length of stay was not
279 significantly changed. Hospital stay relies on various factors, which may modify to a
280 certain extent the effect of perioperative care and different analgesic regimens in
281 particular²⁴. Logistic and economic resources differ between countries and
282 institutions and socio-cultural differences cannot be neglected; comparison of
283 hospital stay can therefore be misleading. Medical recovery is the more specific
284 endpoint that tends to occur about 2 days before discharge as shown by our group
285 and by others²⁵. Actually, only Levy et al. reported significantly shorter hospital stay
286 in patients with PCA¹⁶, while several other randomized studies comparing EDA vs.
287 PCA for laparoscopic colorectal resections did not find any difference⁹⁻¹¹. Small
288 patient samples however limit those trials. Levy reported further extremely short
289 postoperative stays of 2.7 days only in patients with PCA¹⁶. Proven benefits of EDA
290 for major and especially open procedures (e.g. superior pain relief, reduction of
291 cardiopulmonary complications, faster bowel recovery)⁸ are probably minor and

292 irrelevant for minimal-invasive procedures with very short stays^{14, 16}; this being said,
293 minor drawbacks like pruritus and especially transitory hypotension become
294 problematic and may increase stay at a high dependency unit and slow down
295 recovery as shown in the present study and observed by others^{8, 9, 16, 31, 32}.

296 Colon and rectal surgery differ considerably in terms of technique, surgical
297 trauma and early outcomes. The most recent ERAS[®] recommendations were
298 therefore issued separately for the two entities^{4, 5}. While the available data from the
299 present study and previous ones appears to be sufficient to abandon EDA for
300 laparoscopic *colon* resections, evidence is insufficient to for *rectal* resections as the
301 collectives in the respective randomized trials are too small^{9, 10, 16}.

302 EDA failed in 12% of the patients in our study and was removed in 28%
303 patients after anticipated POD 2. These “deviations” disfavor the EDA group on the
304 one hand but reflect clinical realities on the other hand^{8, 33}. Further, epidural
305 analgesia can be performed at different thoracic levels, and combination and
306 concentration of medications vary considerably. The results of our study can
307 therefore not be uncritically generalized to other settings. However, the institutional
308 technique applied in the present study and the reported success rates were in line
309 with recent publications and might therefore still be of interest for many institutions^{8,}
310 ^{20, 33}. Several interesting alternatives for perioperative pain management have been
311 suggested meanwhile and favorable results have been reported in particular for
312 laparoscopic transverse abdominus plane blocks, wound infiltration, systemic
313 steroids and systemic lidocaine^{17, 18}.

314

315 Several limitations need to be addressed. Both groups were well matched by
316 means of randomization. However, EDA patients experienced more overall and
317 major complications than patients with PCA. These were mainly unrelated

318 complications entailing a potential bias disfavoring the EDA group. Therefore,
319 patients with major complications were excluded in a *post hoc* subgroup analysis
320 because of an obvious impact on outcome. Postoperative pain management is
321 embedded in a global care scheme and the impact of EDA or other modalities on
322 recovery, pain relief and length of stay needs to be interpreted in this context. As
323 mentioned in the methods section, the enhanced recovery pathway was adapted
324 during the study period. In order to avoid the bias of various perioperative care
325 pathways and unbalanced major complications, a second subgroup analysis was
326 performed with all consecutive patients within the full ERAS[®] pathway and without
327 major complications. The interesting point was that both subgroup analyses
328 confirmed the results of the main analysis according to the intention-to-treat principle,
329 and resulted in significantly reduced times for medical recovery and high dependency
330 stay in PCA patients.

331
332 In conclusion, the present study suggests that epidurals decrease blood
333 pressure in about one third of patients who therefore require transitory hemodynamic
334 support and a prolonged stay in a high dependency unit. Thus, EDA impedes
335 recovery after laparoscopic colorectal resections without providing superior pain relief
336 or reduced complications when compared with morphine-based PCA. Hospital stay
337 remains unchanged. EDA should therefore not be a mandatory item of ERAS[®]
338 pathways in laparoscopic surgery. The most recent ERAS[®] recommendations
339 already considered the new evidence^{4,5}, and modern alternatives to morphine-based
340 regimens deserve future investigations.

341

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347

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349

350

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Table 1 Demographic and surgical details comparing patients with epidural vs. patient-controlled analgesia.

	EDA	PCA	P
	N=65	N=57	
Age (years)	63.1±15.1	61.2±17.8	0.529
Male gender (%)	37 (57%)	34 (60%)	0.854
BMI (kg/m²)	25.9±5.1	25.5±4.2	0.980
ASA I/II/III	6/49/10	7/41/9	0.853
Charlson	3.2±3.3	3.2±3.8	0.822
Malignant/benign disease	43/22	37/20	0.518
Type of surgery			0.904
Left/sigmoid colectomy	30 (46%)	27 (47%)	
Right/ileocecal resection	18 (28%)	13 (23%)	
Rectum/(sub)total	10 (15%)	11 (19%)	
Other	7 (11%)	6 (11%)	
Conversion, No. of (%)	12 (19%)	8 (14%)	0.625
OR time (min)	239±107	235±104	0.832
Estimated blood loss (ml)	232±217	169 ±152	0.095

Mean values ± standard deviation or no. of patients (%).

EDA – epidural analgesia, PCA – patient-controlled opioid-based analgesia, BMI – body mass index, ASA - American Society of Anesthetists, OR time – operation room time.

Online appendix A Postoperative complications by severity.

	EDA	PCA	P
	N=65	N=57	
No. of patients (%) with			
Any complication	35 (54%)	19 (33%)	0.029
Grade I	4	4	
Grade II	16	10	
Grade III a/b	2 / 9	0 / 2	
Grade IV a/b	0 / 2	3 / 0	
Grade V (mortality)	2	0	
Major complications (≥III)	15 (23%)	5 (9%)	0.213
Reoperation	9 (14%)	4 (7%)	0.254

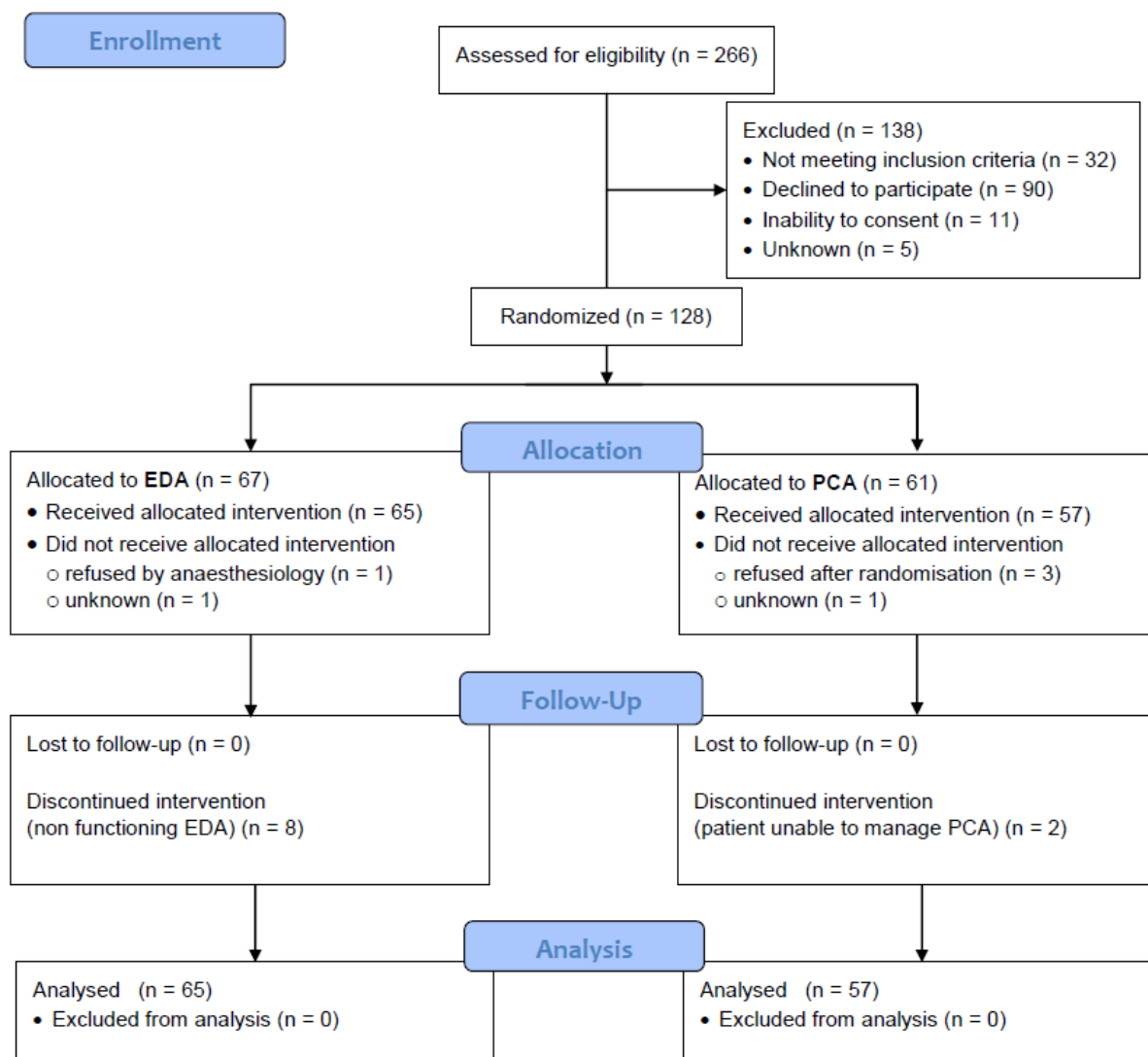
Postoperative complications were graded by severity according to the Dindo-Clavien classification²⁶. Complications grade III-V were summarized as major morbidity.

EDA – epidural analgesia, PCA – patient-controlled opioid-based analgesia.

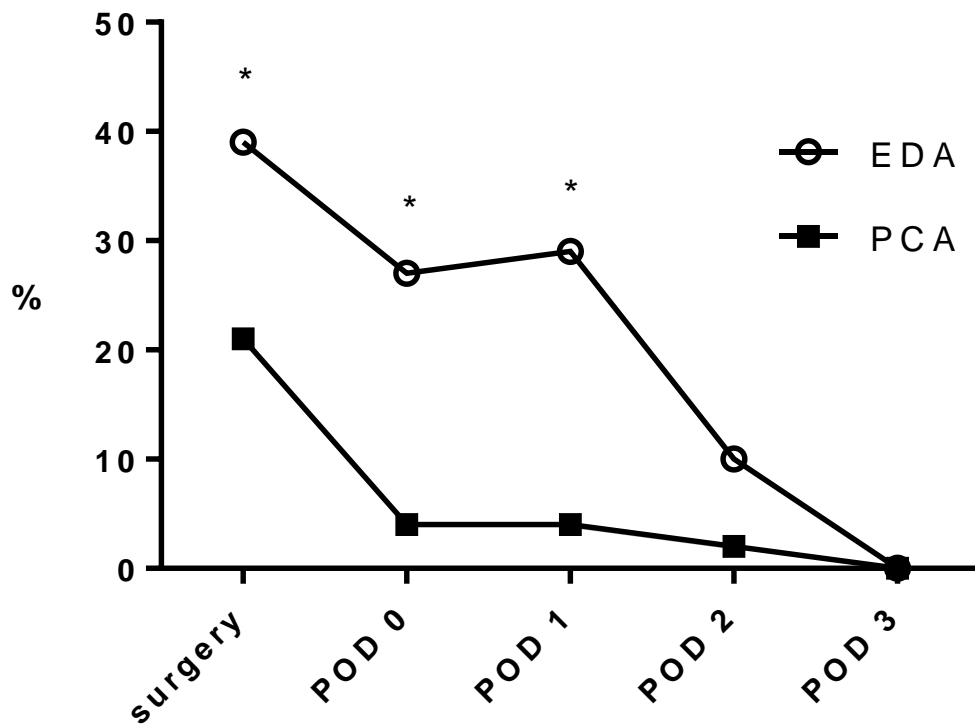
Online appendix B List of surgical and medical complications.

	EDA	PCA
	N=65	N=57
Surgical	21	10
Anastomotic leak	4	1
Bleeding	0	1
Surgical site infection	2	0
Ileus	13	5
Other	2	3
Medical	14	9
Pulmonary	1	1
Cardiac	1	0
Renal	3	2
Urinary retention	11	7
Other	3	5

The most frequent postoperative complications are summarized for patients with epidural analgesia (EDA) and patient-controlled opioid-based analgesia (PCA).

Figure 1 Study flow chart.

CONSORT diagram. Randomized controlled trial comparing epidural analgesia (EDA) *versus* patient-controlled opioid-based analgesia (PCA) for laparoscopic colorectal surgery.

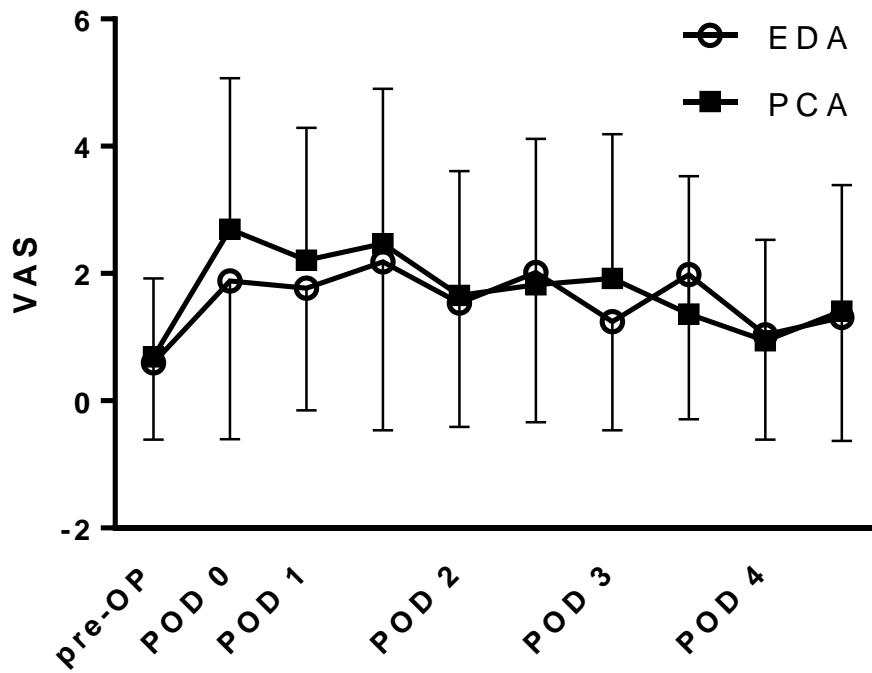
Figure 2 Perioperative vasopressor requirements.

Percentage of patients in the EDA (white circles) and PCA group (black rectangles), respectively, requiring vasopressor treatment during and after laparoscopic colorectal surgery.

EDA – epidural analgesia, PCA – patient-controlled opioid-based analgesia.

* indicates statistical significance ($P < 0.05$).

Figure 3 Perioperative pain scores.



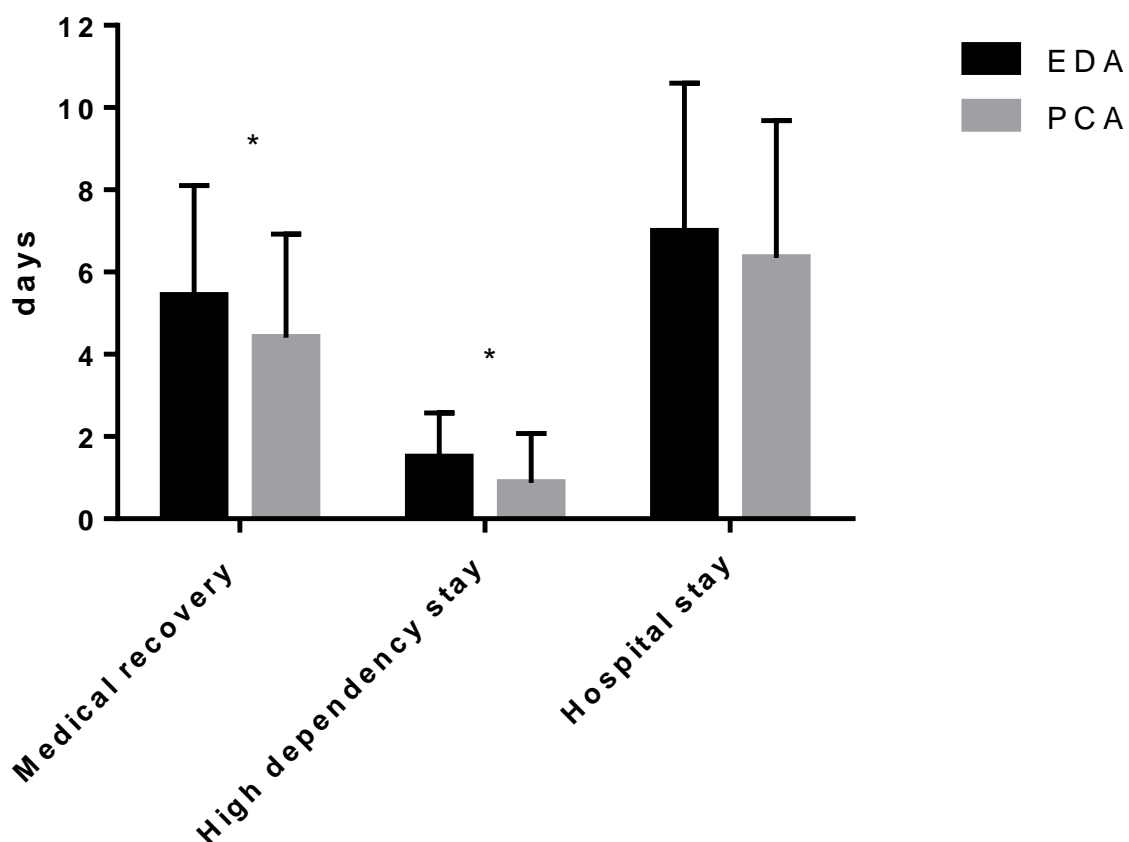
Pain was assessed by use of a visual analogue scale (VAS) from 0-10 before surgery, the evening after surgery and twice daily thereafter until postoperative day (POD) 4 for patients with EDA (white circles) and PCA (black rectangles), respectively.

EDA – epidural analgesia, PCA – patient-controlled opioid-based analgesia.

* indicates statistical significance ($P < 0.05$).

Data expressed as mean \pm SD.

Figure 4 Subgroup analysis excluding patients with major complications.



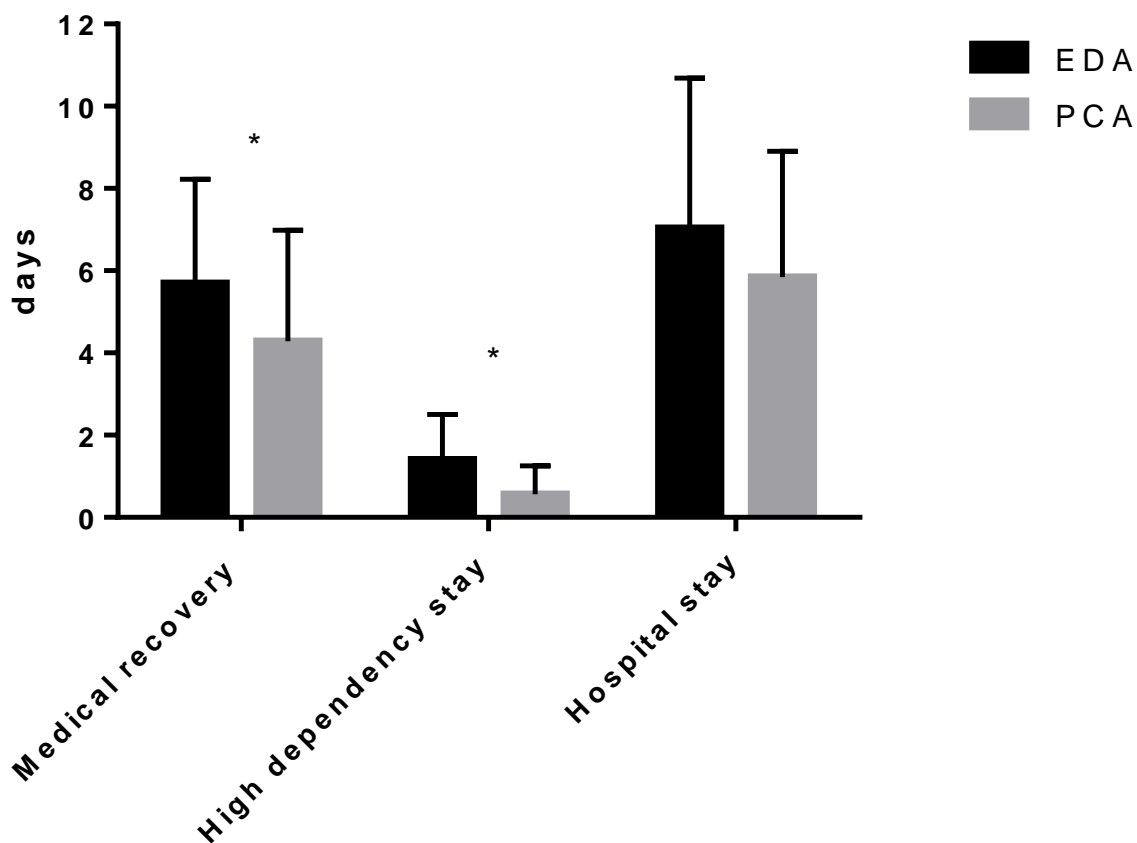
A *Post hoc* subgroup analysis included all patients without major complications: 50 EDA patients vs. 52 PCA patients were compared with regards to medical recovery, and length of stay in a high dependency unit and in hospital, respectively.

EDA – epidural analgesia, PCA – patient-controlled opioid-based analgesia.

* indicates statistical significance ($P < 0.05$).

Data expressed as mean \pm SD.

Online appendix C Subgroup analysis: patients with full ERAS[®] pathway and having no major complications.



Patients within the full ERAS[®] pathway and without major complications (40 EDA vs. 40 PCA) were compared concerning medical recovery, high dependency and hospital stay.

EDA – epidural analgesia, PCA – patient-controlled opioid-based analgesia.

* indicates statistical significance (P < 0.05).

Data expressed as mean ± SD.