

3 ORIGINAL ARTICLE

4 Comparison of 0.25% and 0.125% 5 bupivacaine in hyperthermic 6 intraperitoneal chemotherapy (HIPEC): 7 a single-center experience

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10 ABSTRACT

11 **Background:** Cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) causes
12 severe postoperative pain; thoracic epidural analgesia is recommended, but the optimal epidural bupivacaine
13 concentration has not been studied in this setting. We compared 0.25% and 0.125% epidural bupivacaine
14 after CRS + HIPEC.

15 **Methodology:** This retrospective cohort study included 77 adults who underwent CRS + HIPEC at a tertiary
16 care center between January 2017 and December 2021. All received epidural fentanyl 2 mcg/ml with 0.125%
17 ($n = 59$) or 0.25% ($n = 18$) bupivacaine (non-randomized). Pain severity was categorized from visual analog
18 scale assessments. Secondary outcomes were sensory block level, supplementary intravenous (IV) analgesia,
19 patient-controlled analgesia (PCA), and adverse effects. Groups were compared using Fisher's exact or Fisher-
20 Freeman-Halton exact tests.

21 **Results:** Mild pain occurred in 11/18 patients (61.1%) receiving 0.25% and 19/59 (32.2%) receiving 0.125%
22 bupivacaine (exploratory risk difference 28.9 percentage points; 95% confidence interval 3.1–50.3), moderate
23 pain in 7 (38.9%) and 38 (64.4%), and severe pain in 0 and 2 (3.4%), respectively. The overall pain-severity
24 distribution did not differ significantly ($p = 0.101$), nor did sensory block level ($p = 0.284$), supplementary IV
25 analgesia ($p = 0.272$), PCA use ($p = 1.000$), or nausea and vomiting ($p = 0.556$). No patient had pruritus or
26 motor complications.

27 **Conclusion:** No statistically significant differences in pain outcomes or adverse effects were detected between
28 the two concentrations. The small, unequal, and non-randomized groups preclude conclusions about equiva-
29 lence or superiority; adequately powered prospective studies are needed.

30 **Keywords:** Cytoreductive surgery, hyperthermic intraperitoneal chemotherapy, epidural analgesia, bupiv-
31 acaine, postoperative pain.

32 Introduction

33 Peritoneal surface malignancies are routinely treated
34 with cytoreductive surgery (CRS) and hyperthermic
35 intraperitoneal chemotherapy (HIPEC) [1]. After
36 complete macroscopic disease has been surgically
37 resected, chemotherapy heated to 42°C is perfused
38 into the abdominal cavity, where hyperthermia and the
39 pharmacokinetic benefit of the intraperitoneal route
40 synergize to improve penetration into microscopic disease
41 while minimizing systemic toxicity [1,2]. The operation
42 is long and physiologically demanding. It involves a
43 xiphoid-to-pubis laparotomy, extensive peritonectomy,

multivisceral resection, major fluid shifts, and a period of 44
induced hyperthermia, and it causes severe postoperative 45
pain and substantial morbidity [3,4]. 46

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51	Pain after CRS + HIPEC is more intense and more	112
52	prolonged than after comparable open abdominal	113
53	surgery. This reflects the length of the incision, the extent	114
54	of peritoneal stripping and visceral handling, and the	115
55	chemical peritonitis generated by the heated perfusate;	116
56	analgesic requirements frequently extend well beyond	117
57	the conventional 48–72 hours [3,4]. The Enhanced	118
58	Recovery After Surgery (ERAS) Society guidelines for	119
59	CRS ± HIPEC recommend thoracic epidural analgesia	120
60	(TEA) as the standard technique in the absence of	
61	contraindications [4–7]. TEA provides superior dynamic	121
62	pain control and lowers systemic opioid requirements,	122
63	and it is the main technique for postoperative analgesia	123
64	after CRS + HIPEC [4,6,7].	124
65	Bupivacaine is one of the most commonly used local	125
66	anesthetics administered via the epidural route [8,9].	126
67	In clinical practice, the sensory–motor profile of	127
68	an epidural infusion is influenced by both the local	128
69	anesthetic concentration and the total dose delivered.	129
70	Lower concentrations produce sensory blockade with	
71	relative motor sparing, whereas higher concentrations	130
72	progressively recruit motor fibers and deepen sympathetic	131
73	blockade [10,11]. This concentration-dependent effect is	132
74	the pharmacological basis for combining a dilute local	133
75	anesthetic with a lipophilic opioid to provide segmental	134
76	analgesia [7,11]. Nausea, vomiting, and pruritus are	135
77	known side effects of epidural analgesia in this population	136
78	and, together with motor blockade, are the adverse effects	137
79	most likely to outweigh any analgesic gain from a higher	138
80	concentration [11].	139
81	Two features of CRS + HIPEC make the choice of	140
82	epidural concentration less straightforward than in routine	
83	abdominal surgery. First, thoracic epidural sympathetic	141
84	blockade can exacerbate, and clinically mimic, the	142
85	hemodynamic effects of HIPEC: hyperthermic perfusion	143
86	markedly reduces systemic vascular resistance and	144
87	causes a hyperdynamic circulation, which compounds	145
88	the hypovolemia and capillary leak caused by extensive	146
89	peritonectomy. This concern has been raised repeatedly	147
90	since the technique was introduced [12–14]. In a large	148
91	cohort, however, most epidural-associated postoperative	
92	hypotensive episodes responded to fluid boluses, and no	149
93	epidural hematomas were reported [15]. Second, CRS +	150
94	HIPEC can disturb coagulation, which directly affects the	151
95	timing of catheter insertion and removal. Intraoperative	152
96	coagulopathy appears limited [16], but postoperative	153
97	thrombocytopenia has been reported around the third	154
98	postoperative day [17] and may delay catheter removal	155
99	[15], so the margin of safety is narrow. The choice of	156
100	epidural bupivacaine concentration may matter clinically	157
101	in these patients.	158
102	Despite this, the concentration of bupivacaine used	159
103	for epidural infusion after CRS + HIPEC has not been	160
104	examined directly. The ERAS recommendation of a low	161
105	concentration of local anesthetic combined with a short-	162
106	acting opioid rests on expert consensus and extrapolation	163
107	from major abdominal surgery rather than on data from this	
108	population [6,7]. In non-HIPEC abdominal and thoracic	164
109	surgery, the most directly relevant comparison remains a	165
110	randomized double-blind trial in which 0.125% or 0.25%	
111	bupivacaine was added to an epidural fentanyl infusion:	166
	the higher concentration conferred no additional analgesia	167
	but produced significantly more sensory loss and a denser	
	motor block, with some patients reaching Bromage grade	
	2–3 [10]. Obstetric studies reported similar analgesia	
	[18,19]; the cesarean cohort reported more hypotension	
	with 0.25% bupivacaine, but its groups also received	
	different lidocaine concentrations, so this difference cannot	
	be attributed to bupivacaine alone [19]. Their applicability	
	to prolonged TEA after CRS + HIPEC is limited.	
	Practice consequently varies widely between institutions	
	[20,21]. A higher concentration might provide a denser	
	sensory block to counter the substantial inflammatory	
	and nociceptive load of the heated perfusate. Conversely,	
	higher concentrations of bupivacaine may cause more	
	motor blockade and hypotension in patients already at	
	risk of vasoplegia, prolonged immobilization, and venous	
	thromboembolism, which could delay mobilization and	
	recovery [22,23].	
	This study therefore aimed to compare postoperative	
	analgesia and adverse effects between 0.25% and	
	0.125% epidural bupivacaine, each combined with	
	fentanyl, in patients undergoing CRS + HIPEC at a	
	single tertiary center in Saudi Arabia. Specifically, we	
	compared pain severity derived from visual analog	
	scale (VAS) assessments, sensory block level, the use of	
	supplementary intravenous (IV) analgesia and patient-	
	controlled analgesia (PCA), and the incidence of nausea	
	and vomiting, pruritus and motor complications between	
	the two concentrations.	
	Subjects and Methods	
	<i>Study design and setting</i>	
	This retrospective cohort study reviewed the electronic	
	medical records (EMRs) of all consecutive adult patients	
	who underwent CRS + HIPEC at a single tertiary care	
	center in Saudi Arabia between January 2017 and	
	December 2021. CRS + HIPEC is routinely performed	
	at this center.	
	Participants	
	Patients were eligible if they were aged 18 years or	
	older, underwent CRS + HIPEC during the study	
	period, received epidural analgesia with either 0.25%	
	or 0.125% bupivacaine during the perioperative period,	
	and had medical records documenting postoperative	
	analgesia and pain assessment. Patients were excluded	
	if the bupivacaine concentration or postoperative pain	
	assessments were not documented, if they received	
	additional or alternative local anesthetics during the	
	perioperative period, or if they had conditions likely to	
	influence pain outcomes, such as chronic pain syndromes	
	or opioid dependence. Eligible patients were grouped	
	according to the epidural bupivacaine concentration they	
	received (0.25% or 0.125%).	
	<i>Epidural analgesia regimen and treatment</i>	
	<i>allocation</i>	
	All patients received an epidural infusion of bupivacaine	
	(0.25% or 0.125%) combined with fentanyl 2 mcg/ml.	

168 Bupivacaine concentration was not randomly assigned;
169 both 0.25% and 0.125% were in use throughout the study
170 period, and the choice was made according to the practice
171 preference of the attending anesthesiologist.

172 **Data collection and outcome definitions**

173 Data were extracted from the EMRs using a standardized
174 data collection form and entered into a secure database.
175 Recorded variables included postoperative VAS pain
176 assessments, duration of epidural infusion, infusion
177 rate, use of supplementary IV analgesics and PCA, the
178 sensory level of the epidural block (range T4–T10), and
179 adverse effects, namely nausea and vomiting, pruritus,
180 and motor complications. Pain severity was categorized
181 from each patient's recorded postoperative VAS score
182 (0–10 scale) using standard clinical VAS cut-offs: mild
183 (1–3), moderate (4–6), and severe (7–10). No patient had
184 a recorded VAS score of 0 (no pain), so every patient
185 was assigned to one of these three categories. The overall
186 mean VAS was calculated from these patient-level scores.

187 **Statistical analysis**

188 Continuous variables are presented as mean $\pm$ standard
189 deviation (SD) and categorical variables as frequencies and
190 percentages; in between-group comparisons, percentages
191 were calculated within each bupivacaine group. 95%
192 confidence intervals (CIs) for individual proportions were
193 calculated using the Wilson score method.

194 Categorical variables were compared between the 0.25%
195 and 0.125% groups using Fisher's exact test for 2×2
196 tables and the Fisher–Freeman–Halton exact test for larger
197 contingency tables (pain severity, three categories; sensory
198 block level, seven categories), with p values estimated
199 by Monte Carlo simulation based on 200,000 resamples.
200 Pain was compared between groups using the VAS-
201 derived severity categories, and the overall mean VAS is
202 reported descriptively for the cohort. The between-group
203 difference in the proportion of patients with mild pain was
204 summarized as an exploratory risk difference with a 95%
205 CI calculated using the Newcombe method; this contrast
206 was not treated as a confirmatory outcome. A two-sided p
207 value < 0.05 was considered statistically significant. All
208 statistical analyses were conducted using SPSS software
209 (version 26.0; IBM Corp., Armonk, NY, USA).

210 **Ethical approval**

211 The study was approved by the institutional review board
212 of the study center (approval details are provided on the
213 title page), which waived the requirement for informed
214 consent because of the retrospective design. Patient data
215 were stored in an encrypted database accessible only to
216 authorized study personnel, and findings are reported in
217 aggregate without personally identifiable information.

218 **Results**

219 Of 93 patients initially identified as having undergone
220 CRS + HIPEC during the study period, 16 were
221 excluded because of incomplete medical records: the
222 bupivacaine concentration was not documented in
223 3 patients, postoperative pain assessments were not

documented in 5, and both were missing in 8, leaving 224
77 patients for analysis. Of these, 18 (23.4%) received 225
0.25% bupivacaine and 59 (76.6%) received 0.125% 226
bupivacaine. 227

Table 1 summarizes the characteristics of the 77 included 228
patients. All patients received epidural analgesia with 229
bupivacaine combined with fentanyl 2 mcg/ml, at a mean 230
infusion rate of 7.2 ± 2.3 ml/h, and the mean duration 231
of epidural infusion was 4 ± 1.4 days. Supplementary 232
IV analgesia was given to 66 patients (85.7%), and one 233
patient (1.3%) received PCA. The cohort mean VAS 234
score was 4 ± 1.2 . 235

Overall, 45 patients (58.4%) had moderate pain, 30 236
(39.0%) had mild pain and 2 (2.6%) had severe pain. The 237
most common sensory block levels were T6 (25 patients, 238
32.5%), T8 (18, 23.4%), and T4 (17, 22.1%). 239

Nausea and vomiting occurred in three patients (3.9%), 240
and no patient had pruritus or motor complications. 241

Table 2 compares outcomes between the 0.25% and 242
0.125% bupivacaine groups; percentages were calculated 243
within each group. 244

Mild pain was recorded in 11 of 18 patients (61.1%) 245
in the 0.25% group and 19 of 59 (32.2%) in the 0.125% 246
group, moderate pain in 7 of 18 (38.9%) and 38 of 59 247
(64.4%), and severe pain in 0 of 18 (0.0%) and 2 of 59 248
(3.4%), respectively. The overall distribution across the 249
three pain-severity categories did not differ significantly 250
between groups (Fisher–Freeman–Halton exact test, $p =$ 251
0.101). The exploratory risk difference for mild pain was 252
28.9 percentage points (95% CI 3.1–50.3); although this 253
interval excludes zero, it concerns a single category of a 254
three-category outcome whose overall comparison was not 255
statistically significant, and it was therefore not interpreted 256
as confirmatory. Supplementary IV analgesia (14 of 18, 257
77.8% vs. 52 of 59, 88.1%; Fisher's exact test, $p = 0.272$) 258
and PCA use (0 of 18, 0.0% vs. 1 of 59, 1.7%; Fisher's exact 259
test, $p = 1.000$) did not differ significantly between groups. 260

The distribution of sensory block levels did not differ 261
significantly between groups (Fisher–Freeman–Halton 262
exact test, $p = 0.284$). The most common level was T8 in 263
the 0.25% group (7 of 18, 38.9%) and T6 in the 0.125% 264
group (20 of 59, 33.9%). Nausea and vomiting occurred 265
in 1 of 18 patients (5.6%) in the 0.25% group and 2 of 59 266
(3.4%) in the 0.125% group (Fisher's exact test, $p = 0.556$). 267

268 **Discussion**

In this retrospective cohort of 77 patients who underwent 269
CRS + HIPEC, epidural analgesia using 0.125% and 270
0.25% bupivacaine combined with fentanyl showed 271
no statistically significant differences in the recorded 272
postoperative pain-severity distribution, sensory block 273
distribution, postoperative nausea and vomiting, 274
or supplemental analgesic requirements. No motor 275
complications were recorded in either group. The 0.25% 276
group had a higher proportion of patients with mild pain, 277
but the overall three-category pain-severity comparison 278
was not statistically significant. 279

Since both groups received epidural fentanyl, the 280
opioid component may have contributed substantially 281

Table 1. Characteristics of the study cohort (N = 77).

Variable	Value
Epidural analgesia, n (%)	Yes: 77 (100%)
PCA, n (%)	No: 76 (98.7%); Yes: 1 (1.3%)
Supplementary IV analgesia, n (%)	No: 11 (14.3%); Yes: 66 (85.7%)
Duration of epidural infusion (days), mean $\pm$ SD	4 $\pm$ 1.4
VAS pain score, mean $\pm$ SD	4 $\pm$ 1.2
Pain severitya, n (%)	Mild: 30 (39.0%); moderate: 45 (58.4%); severe: 2 (2.6%)
Bupivacaine concentration, n (%)	0.25%: 18 (23.4%); 0.125%: 59 (76.6%)
Epidural fentanyl concentration	2 mcg/ml in all patients (77, 100%)
Epidural infusion rate (ml/h), mean $\pm$ SD	7.2 $\pm$ 2.3
Sensory block level, n (%)	T4: 17 (22.1%); T5: 4 (5.2%); T6: 25 (32.5%); T7: 4 (5.2%); T8: 18 (23.4%); T9: 5 (6.5%); T10: 4 (5.2%)
Nausea and vomiting, n (%)	No: 74 (96.1%); Yes: 3 (3.9%)
Pruritus, n (%)	No: 77 (100%)
Motor complications, n (%)	No: 77 (100%)

Data are n (%) or mean $\pm$ SD. ^aPain severity categories were derived from each patient's recorded VAS score (0–10): mild, 1–3; moderate, 4–6; severe, 7–10. Abbreviations: IV, intravenous; PCA, patient-controlled analgesia; SD, standard deviation; T, thoracic dermatome level; VAS, visual analog scale.

Table 2. Comparison of outcomes between 0.25% and 0.125% epidural bupivacaine (N = 77).

Variable	0.25% bupivacaine (n = 18)	0.125% bupivacaine (n = 59)	Test; p value
PCA – No	18 (100.0%, 95% CI 82.4%–100%)	58 (98.3%, 95% CI 91.0%–99.7%)	Fisher's exact test; p = 1.000
PCA – Yes	0 (0.0%, 95% CI 0%–17.6%)	1 (1.7%, 95% CI 0.3%–9.0%)	
Supplementary IV analgesia – No	4 (22.2%, 95% CI 9.0%–45.2%)	7 (11.9%, 95% CI 5.9%–22.5%)	Fisher's exact test; p = 0.272
Supplementary IV analgesia – Yes	14 (77.8%, 95% CI 54.8%–91.0%)	52 (88.1%, 95% CI 77.5%–94.1%)	
Pain severitya – Mildc	11 (61.1%, 95% CI 38.6%–79.7%)	19 (32.2%, 95% CI 21.7%–44.9%)	Fisher–Freeman–Halton exact testb; p = 0.101
Pain severitya – Moderate	7 (38.9%, 95% CI 20.3%–61.4%)	38 (64.4%, 95% CI 51.7%–75.4%)	
Pain severitya – Severe	0 (0.0%, 95% CI 0%–17.6%)	2 (3.4%, 95% CI 0.9%–11.5%)	
Sensory block level – T4	2 (11.1%)	15 (25.4%)	Fisher–Freeman–Halton exact testb; p = 0.284
Sensory block level – T5	1 (5.6%)	3 (5.1%)	
Sensory block level – T6	5 (27.8%)	20 (33.9%)	
Sensory block level – T7	2 (11.1%)	2 (3.4%)	
Sensory block level – T8	7 (38.9%)	11 (18.6%)	
Sensory block level – T9	0 (0.0%)	5 (8.5%)	
Sensory block level – T10	1 (5.6%)	3 (5.1%)	
Nausea and vomiting – No	17 (94.4%, 95% CI 74.2%–99.0%)	57 (96.6%, 95% CI 88.5%–99.1%)	Fisher's exact test; p = 0.556
Nausea and vomiting – Yes	1 (5.6%, 95% CI 1.0%–25.8%)	2 (3.4%, 95% CI 0.9%–11.5%)	

Data are n (%; 95% CI) or n (%). Percentages are calculated within each group; 95% CIs for proportions were calculated using the Wilson score method. ^aPain severity categories were derived from VAS assessments as defined in the Table 1 footnote.

^bP value for the overall comparison across all categories of the variable; Fisher–Freeman–Halton p values are Monte Carlo estimates based on 200,000 resamples.

^cExploratory risk difference for mild pain (0.25% minus 0.125%): 28.9 percentage points (95% CI 3.1–50.3; Newcombe method). This single-category contrast was not treated as a confirmatory comparison.

Abbreviations: CI, confidence interval; IV, intravenous; PCA, patient-controlled analgesia; T, thoracic dermatome level; VAS, visual analog scale.

to analgesia in both groups and may have reduced differences attributable to bupivacaine concentration alone. The overall mean VAS score of approximately 4 also indicates that pain was generally controlled at a moderate level across the cohort. Because between-group comparisons were based on VAS-derived categories

rather than continuous scores, these results should not be interpreted as evidence for or against a difference in mean VAS scores.

The mild-pain finding requires cautious interpretation. The exploratory risk difference of 28.9 percentage points was imprecise (95% CI 3.1–50.3), as the 0.25% group

294 was small, and the overall comparison across the three
295 pain-severity categories was not statistically significant
296 ($p = 0.101$). Because bupivacaine concentration was not
297 randomly assigned, this difference may reflect differences
298 in patient or clinical characteristics between the groups
299 rather than an effect of concentration. It should therefore
300 be regarded as hypothesis-generating.

301 These results are consistent with the closest non-HIPEC
302 trial identified, in which 0.25% bupivacaine combined
303 with epidural fentanyl did not provide a pain-relief
304 advantage over 0.125% but led to more sensory loss and a
305 denser motor block [10]. Obstetric evidence is limited: a
306 labor trial found no significant difference in pain scores or
307 motor block [18], while a cesarean cohort reported more
308 hypotension with the higher bupivacaine concentration
309 but also used different lidocaine concentrations [19].
310 These studies do not establish a preferred concentration
311 after CRS + HIPEC.

312 Most of the existing CRS + HIPEC literature has
313 compared different analgesic techniques, such as TEA
314 versus transversus abdominis plane block [21] or IV
315 lidocaine infusion [22,23]. There is little direct evidence
316 on the optimal concentration of epidural bupivacaine
317 for this patient group. The present study addresses this
318 specific, clinically adjustable question while keeping the
319 analgesic technique consistent.

320 This question is relevant because TEA in CRS + HIPEC
321 has been linked to sympathetic blockade, hypotension
322 and coagulation-related concerns [12–15,17], and higher
323 bupivacaine concentrations produce denser motor
324 block [10]. Higher concentrations may also increase
325 sympathetic blockade, although direct evidence is
326 limited; in a randomized trial comparing low- and high-
327 concentration epidural levobupivacaine after lower
328 abdominal surgery, analgesia was similar with both
329 concentrations, total dose rather than concentration
330 appeared to determine analgesic quality, and motor block
331 was more frequent with continuous infusion than with
332 patient-controlled boluses [24]. No motor complications
333 were recorded in either group in our cohort; however,
334 given the small sample, the low event rates and the
335 absence of systematically recorded hemodynamic data,
336 this observation does not permit conclusions about the
337 comparative safety of the two concentrations.

338 Our findings do not provide grounds for changing current
339 recommendations. The ERAS Society guidance favors a
340 dilute local anesthetic combined with a lipophilic opioid,
341 which may reduce motor and sympathetic blockade
342 [4,6,7]; the present data neither confirm nor refute this
343 recommendation. The absence of statistically significant
344 between-group differences in this small retrospective
345 cohort does not establish that 0.125% and 0.25%
346 bupivacaine are equally effective or equally safe, or that
347 either concentration is preferable.

348 Larger prospective studies are needed to determine
349 whether the higher proportion of mild pain in the 0.25%
350 group is reproducible and to define the optimal epidural
351 bupivacaine concentration for CRS + HIPEC.

352 Our study has several strengths. To our knowledge,
353 few studies have directly compared 0.125% with

0.25% epidural bupivacaine in CRS + HIPEC, where
concentration recommendations rest on consensus and
extrapolation from other populations [6]. It reflects
routine practice in a tertiary center at a time when
analgesic practice varies widely between institutions
[20,21]. The cohort is procedurally homogeneous, as all
patients underwent CRS + HIPEC, unlike earlier trials in
other surgical populations [10,24].

This study has several limitations. First, its retrospective
single-center design increases the potential for selection
bias and unmeasured confounding. In particular, patients
were not randomized to bupivacaine concentration.
Although the concentration was chosen according to the
practice preference of the attending anesthesiologist rather
than a protocol based on patient characteristics, clinicians
may still have considered individual patient factors,
so confounding by indication and other unmeasured
confounding cannot be excluded, and the sample was too
small for multivariable adjustment. Baseline demographic
and clinical characteristics were not captured in the
study dataset, so the comparability of the groups could
not be assessed. Second, the small and unequal group
sizes (18 vs. 59 patients) reduced statistical power, and
the absence of statistically significant differences should
not be interpreted as evidence of equivalence. Third,
postoperative outcomes were limited to routinely recorded
clinical data. Serial pain ratings, total opioid consumption,
hemodynamic variables, and functional recovery markers
were not consistently available; pain was analyzed from
a single recorded VAS score per patient and compared
between groups only as severity categories, not as mean
scores, so a comprehensive assessment of analgesic
efficacy and safety was not possible. Fourth, adverse
events were infrequent, which precludes meaningful
conclusions about comparative safety. Future adequately
powered multicenter randomized trials should predefine
hemodynamic endpoints, such as the incidence and
duration of hypotension and vasopressor requirements
during the hyperthermic phase [12–14], quantify analgesia
using patient-level dynamic pain scores and opioid
consumption, and include functional and patient-reported
recovery outcomes relevant to ERAS pathways [6,21].

Conclusion

In this retrospective cohort of patients who underwent
CRS + HIPEC at a single center, epidural infusions
of 0.25% and 0.125% bupivacaine combined with
fentanyl were not associated with statistically significant
differences in the recorded postoperative pain-severity
distribution or adverse effects. Although a higher
proportion of patients receiving 0.25% bupivacaine had
mild pain, the overall pain-severity comparison was not
statistically significant. Given the small, unequal and
non-randomized groups, these findings do not establish
the equivalence or superiority of either concentration.
Larger prospective randomized studies are needed to
determine the optimal epidural bupivacaine concentration
for patients undergoing CRS + HIPEC.

List of Abbreviations

CI Confidence interval;
CRS Cytoreductive surgery;

- 414 EMR Electronic medical record;
 - 415 ERAS Enhanced Recovery After Surgery;
 - 416 HIPEC Hyperthermic intraperitoneal chemotherapy;
 - 417 IV Intravenous;
 - 418 PCA Patient-controlled analgesia;
 - 419 TEA Thoracic epidural analgesia;
 - 420 VAS Visual analog scale.
- 421 **Conflict of interests**
- 422 The authors declare that there is no conflict of interest
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- 431 Institutional Review Board because of the retrospective
- 432 design of the study.
- 433 **Ethical Approval**
- 434 Ethical approval was granted by the Institutional Review
- 435 Board of King Khalid University Hospital, King Saud University,
- 436 Riyadh, Saudi Arabia, via approval no. R26-IRB-707, dated: 3
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- 446 *Supplementary content (If any) is available online.*
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