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Influence of pre-peritoneal vs. epidural levobupivacaine infusion on troponin I and BNP as predictors of cardiac injury in cancer patients undergoing major upper abdominal operations: A randomized controlled clinical trial

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ABSTRACT

Background: Cancer patients undergoing major noncardiac surgery are more likely to experience perioperative morbidity and mortality due to myocardial damage.

Methods: Comparative study enrolled 80 patients with upper abdominal malignancies subjected to major abdominal surgeries. Of them, seventy-two patients were eligible and randomly assigned into two groups; Epidural catheter group ($n = 37$), received thoracic epidural infusion of levobupivacaine, and pre-peritoneal catheter group ($n = 35$), received preperitoneal infusion of levobupivacaine postoperatively. Primary endpoint was pain severity by NRS immediately after recovery, at 2, 4, 6, 12, 24, 36, and 48 hours. Secondary endpoints were: (1) Patient`s hemodynamics monitored for postoperative 48 hours. (2) Myocardial injury, confirmed by troponin I & BNP levels preoperatively and on postoperative day 1 and 2 (3) Time of first analgesic demand and total postoperative 48 h morphine consumption. (4) Cardiovascular side effects; hypotension, bradycardia & arrhythmia. (5) Morphine side effects; PONV

Results: NRS scores showed non-significant reduction at most study times between both groups with significant reduction in the ECI group at 6-, 12-, and 24-hour than other group. First analgesic demand was earlier in PCI group than ECI without significant difference, while total 48 h morphine consumption showed a significant reduction in ECI group than PCI group. Hemodynamics were comparable in both groups. Cardiac enzymes, Troponin I and BNP, showed non-significant differences over study time between both groups. Postoperative complications, PONV, were similar in both groups without any significance, but with more cases of hypotension and bradycardia in epidural group. No cases of myocardial injury or heart failure were reported.

Conclusions: Preperitoneal analgesia is an effective analgesic method comparable to epidural analgesia limiting the occurrence of major cardiovascular events in cancer patients undergoing major abdominal surgeries and can be utilized when epidural analgesia is not desired or forbidden.

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Myocardial injury; epidural analgesia; preperitoneal catheter

1. Introduction

Myocardial injury after noncardiac surgery (MINS) is a new pathological entity that occurs in up to 35% of surgical patients and increases the risk of major adverse cardiac events (MACEs); myocardial ischemia and infarction, arrhythmias, heart failure, and cardiac death, resulting in longer hospital stay [1]. It is defined by an increase in plasma CK. MB isoenzyme and troponin I levels in the presence or absence of clinical and electrocardiographic ischemic changes. Troponin has been shown to be a better predictor of postsurgical complications [2]. Furthermore, N-terminal pro-brain natriuretic peptide concentrations dramatically rise following non-cardiac surgery within the first 3 days reflecting an increased myocardial strain. So, it is a validated biomarker for assessing perioperative cardiac function [3].

Patients with abdominal malignancies who undergo major surgery may experience severe postoperative abdominal pain, which exacerbates the patient's general state [4]. Furthermore, surgery is a stressful event linked with catecholamine release, which negatively impacts myocardial function and oxygenation, resulting in sympathetic nervous system activation, cardiovascular, endocrine, and musculoskeletal system diseases, reduced physical fitness, and psychological health [5]. As a result, effective

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postoperative pain management is a critical health priority reducing perioperative myocardial infarction; most significant markers of morbidity and death associated with noncardiac surgery, and enhancing overall outcome [6].

The conventional strategy to postoperative analgesia following laparotomy is multimodal therapy including oral analgesics and PCA or epidural [7]. Thoracic epidural anesthesia has become a standard procedure for surgeries, delivering extremely efficient analgesia. It has the capability to guarantee early movement, speedier recovery of gastrointestinal function, and lower cardiovascular and pulmonary complications following abdominal surgery [8]. However, it has been restricted for a variety of reasons including hypotension, motor blockade, given anticoagulants to avoid complications; epidural hematoma, urine retention, significant failure rates [9], and elderly with degenerated spines and exaggerated hemodynamic response [10].

As a consequence, an optimal strategy is essential for alleviating pain with minimal drug dosage and fewer systemic effects. So, scientists concentrated on establishing the mechanism of incisional pain to design novel models for pain relief [11]. For nearly a decade, TAP block have been advised for postoperative analgesia. It generated somatic analgesia, but analgesia for longer abdominal incisions requires bilateral blocks [12]. This time-limited effect of a single shot of L.A has been overcome by continuous wound infusion using catheters, which has been demonstrated to offer enhanced pain relief [13]. CWI of L.A to the preperitoneal plane has recently gained favor. It avoids the unfavorable implications of neuraxial blocks and adverse effects of opioids, provides long-lasting analgesia, and most importantly, can be administered safely with perioperative anticoagulants [14].

Our aim was to investigate the impact of continuous preperitoneal analgesia versus epidural analgesia on the occurrence of major cardiovascular events in cancer patients who underwent major upper abdominal surgeries.

2. Patient and method

Our cancer institute conducted this randomized prospective comparative study, after obtaining approval from the cancer`s Institutional Review Board (Approval Number: 440), in accordance with CONSORT criteria once each patient has provided written permission. The trial was registered at ClinicalTrials.gov with the unique ID number NCT04152564. It began on 29 October 2018 and ended on 8 September 2022.

72 patients categorized as ASA class I-III, with age from 20 to 70 years, planned for major abdominal cancer surgeries were incorporated into the study after eighty patients were enrolled and validated for inclusion and exclusion criteria. Patients with ASA class >III, morbid obesity, prior opioid use, inability to use a PCA device, allergy to levobupivacaine, contraindications of epidural analgesia and pregnancy were excluded. A statistician assigned the 72 patients randomly into two groups: ***ECI group*** ($n = 37$), received postoperative thoracic epidural infusion of levobupivacaine, and ***PCI group*** ($n = 35$), received preperitoneal catheter infusion of levobupivacaine postoperatively.

We taught patients before surgery how to rate their pain on NRS, where 0 symbolizes no pain and 10 represents most awful pain, and how to operate the PCA device (Injectomat Master PCA®, Fresenius Kabi, Sèvres, France). Basic monitoring probes were applied in the preoperative room (noninvasive blood pressure, pulse oximetry and 5-lead ECG) to monitor the patient's vital signs. After inserting a wide bore cannula and infusing 1 L of lactate ringer solution, intravenous midazolam 2–3 mg and fentanyl 50 µg were given separately.

Then, patients were placed in a sitting position with fully flexed and thoracic spines and were outlined under strict aseptic precautions. The desired insertion site was T9–10. After that, 3 milliliters of lidocaine 1% were infiltrated at the needle insertion site, and a Tuohy epidural needle 18 G was inserted via the paramedian approach. Hanging drop technique was used to verify the epidural space. To capture intrathecal or intravascular misplacement, a test dose of 3 mL of 2% lidocaine containing 1:200,000 adrenaline was injected, then the epidural catheter was passed through the epidural needle to be placed 3–4 cm beyond the needle tip and fixed at a length of 9–12 cm from the skin. Finally, we administered 2 mL of contrast dye via the catheter, followed by anteroposterior and lateral fluoroscopic pictures to confirm epidural location.

Standard general anesthesia was administered to all patients and induced, after five deep breathes, with intravenous fentanyl 1–2 µg/kg, propofol 2 mg/kg and rocuronium 0.65 mg/kg then tracheal intubation was performed. Isoflurane 1–1.5 MAC was used to maintain anesthesia, and rocuronium 0.03 mg/kg was administered according to train of four monitoring by nerve stimulator. Fentanyl 0.5–1 µg/kg was administered intraoperatively, when needed, to keep the blood pressure and heart rate within 20% of the basal value. Central venous catheter was inserted via internal jugular under complete aseptic conditions to monitor central venous pressure (CVP) pre- and postoperatively. Mechanical ventilation was used to keep end tidal CO2 levels 35–40 mmHg. Neuromuscular block was antagonized in all patients at the end of surgery with sugammadex 1–4 mg/kg, and all patients were finally extubated after fulfilling criteria of extubation and adequate train of four reading. Lowering the infusion rate and IV ephedrine 6–12 mg was given for hypotension (mean BP < 60) while atropine 0.01 mg/kg was

administrated for bradycardia (heart rate < 50 beats/min).

At the end of surgery, **in ECI group**, a bolus of 12 ml L-bupivacaine 0.125, was injected through the catheter and then a continuous infusion of 0.1 ml/kg/h of L-bupivacaine 0.125 was delivered at the care unit. While **in PCI Group**, the preperitoneal catheter (CIMPAX C-CAT 15 or 21 cm, Denmark) was positioned by the surgeon above the peritoneum before the closure of the wound 4 cm away from the lower end of the surgical incision through an introducer and secured to the skin ensuring the uniform spread of the local anesthetic in the wound. A 20 ml bolus of L-bupivacaine 0.25% was administered through the catheter and then a continuous fixed infusion rate of 10 ml/h L-bupivacaine 0.25% was delivered using a syringe pump (Perfusor ® B Braun, Germany). When needed, rescue analgesia in the form of IV morphine 1 mg as a bolus dose using PCA device (Injectomat Master PCA®, Fresenius Kabi), with a 5-minute lockout period and without background infusion, was given.

All patients were moved to the surgical ICU after adequate recovery and were monitored 2 days for the following:

- Vital signs (mean blood pressure and heart rate) every 1 hour and CVP at 24 & 48 postoperative hours.
- Pain severity measured by NRS at 0 (immediately postoperative), 2, 4, 6, 12, 24, 36, and 48 postoperative hours.
- 12-lead ECG daily to detect any ischemia.
- Echo-cardiography was made if ischemic attacks were suspected.
- Three venous Blood samples for troponins I and plasma BNP levels were collected in non-pyrogenic, sterile falcon tubes preoperatively, on first and second postoperative days, and if there were any ECG abnormalities suggesting ischemia. BNP was measured on the Architect I System for quantitative determination of BNP. While, plasma Troponin I was measured by a newly developed Elecsys analyzer (fully automated ELISA)

2.1. Primary outcome

Primary outcome was postoperative pain severity by NRS immediately after recovery, at 2, 4, 6, 12, 24, 36, and 48 hours.

2.2. Secondary outcomes

- Patient`s hemodynamics; mean arterial blood pressure, heart rate and CVP monitored for the first 48 postoperative hours.
- Myocardial ischemia or infarction diagnosed clinically or by new ECG ischemic changes and confirmed by echocardiography and cardiac troponin I testing; a level >0.23 ng/mL is regarded the diagnostic cut-off.
- Heart failure, diagnosed clinically and confirmed by detecting B-type natriuretic peptide (BNP) levels; the diagnostic cut-point was 100 pg/mL).
- Time to first analgesic request.
- Total postoperative 48 hours cumulative morphine consumption.
- Cardiovascular Side effects including hypotension, hypertension, bradycardia & dysrhythmia.
- PONV as a morphine side effects

All pain, hemodynamics, and cardiac events were assessed by a resident and documented by nurses who were not aware of the study design. A cardiologist who knew nothing of the study analyzed all ECGs and echocardiogram.

The study sample size was estimated using G* power and sample size calculation 3.1.9.4 based on our primary end point; postoperative pain, which was assessed using mean postoperative NRS data obtained between 0 h and 48 hours following the completion of surgery. In our study, according to a study by Mohamed et al, 2017 [8], a minimum of 29 patients per group are needed with a total of 58 patients, using an effect size 0.759, assuming a power of 81.15% and a type I error of 0.05.

3. Statistical analysis

IBM SPSS Version 23.0. New York was used for statistical analysis of data. Numerical data was investigated for normality by Kolmogorov-Smirnov and Shapiro-Wilk tests. Quantitative variables were described as Mean ± standard deviation or median and range as founded. The student t-test was used to compare regularly distributed data while the Mann-Whitney U test, Wilcoxon Signed Ranks Test, and Freidman test were employed if it was not. Qualitative variables were presented as frequencies and percentages where Chi square test and Fisher Exact test were used for comparison between the groups. Skewed data were presented as median (interquartile range) to compare difference between groups. The significance level was set at $P \leq 0.05$.

4. Results

Seventy-two cancer patients, off 80 participants, underwent major upper abdominal surgeries, were eligible and recruited into the study. Eight patients were excluded; six cases not meeting the inclusion criteria and two cases refused to participate. After that, they were randomly assigned to the ECI group

($n = 37$) and the PCI group ($n = 35$). Following assignment, 12 patients were excluded: one refused the preperitoneal catheter, two refused epidural catheter, two with preperitoneal catheter insertion failure vs one in the ECI group. During follow-up: six patients were excluded; three in both groups due to locally advanced malignancy, two with epidural catheter dislodgement, and one patient due to preperitoneal catheter malposition. Finally, sixty patients (30 in each group) were sustained for analysis (Figure 1).

Demographic characteristics were similar in both groups with no statistically significant differences (Table 1). **Central venous pressure (CVP)** measures were significantly improved over study time in both groups but without any significant differences in between (Table 2). Intraoperative fentanyl

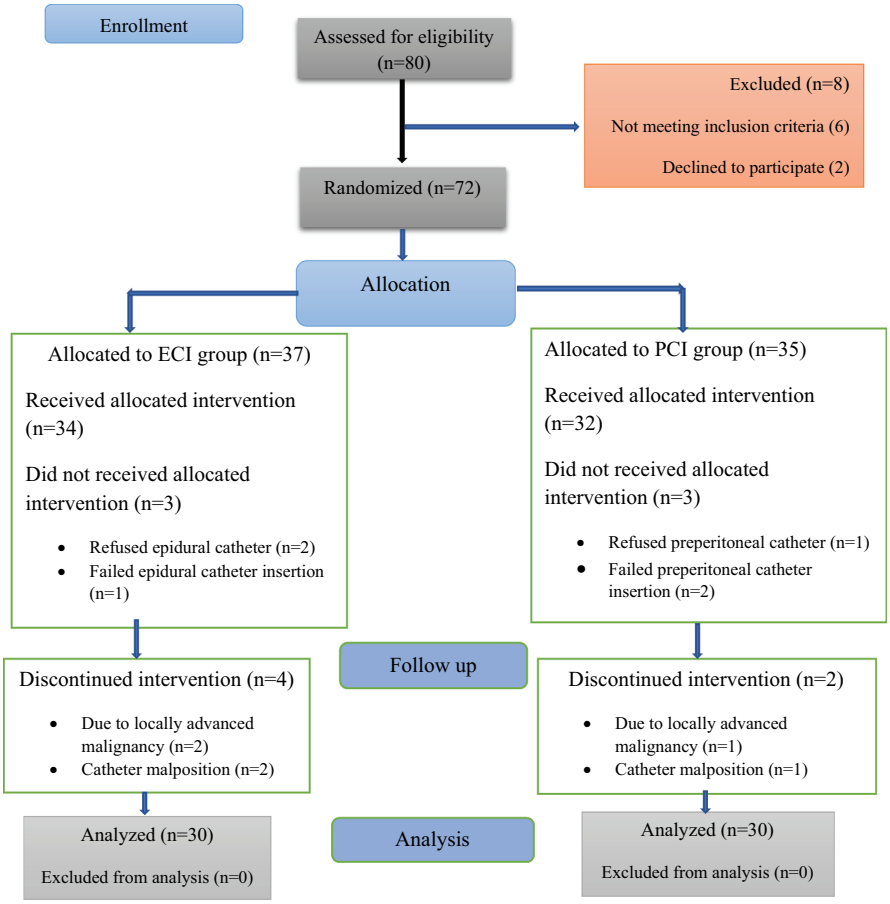

Figure 1. CONSORT flow chart of the participants.

Table 1. Demographic characteristics of two study groups.

	Groups		
	ECI ($n = 30$)	PCI ($n = 30$)	p-value
Sex (n)			
male	12 (40.0%)	14(46.7%)	0.614
female	18 (60.0%)	16 (53.3%)	
Age (y)			
median (range)	61.72 (20.03–70.12)	59.33 (22.08–70.25)	0.489
BMI (kg/m2)			
median (range)	22.84 (17.78–35.44)	24.73 (18.54–35.28)	0.453
Time of Anesthesia (hours)	3.30 (2.30–5.00)	3.73 (2.30–5.00)	0.067
Time of Surgery (hours)	3.00 (2.00–4.45)	3.08 (2.00–4.45)	0.057
Type of operation (n)			
–cancer stomach	10 (33.3%)	6 (20.0%)	0.899
Cancer esophagus	7 (23.3%)	7 (23.3%)	
– Cancer colon	3 (10.0%)	5 (16.7%)	
– Cancer liver	4 (13.3%)	3 (10.0%)	
– Mesenteric mass	1 (3.3%)	1 (3.3%)	
–Renal malignancies	2 (6.7%)	3 (10.0%)	
– Cancer pancreas	2 (6.7%)	2 (6.7%)	
– cancer Gall bladder	1 (3.3%)	3 (10.0%)	
ASA class (n) I/II/III	9/16/5 (30.0%/53.3% /16.7%)	13/14/3 (43.3%/46.7%/10.0%)	0.514

Table 2. CVP over study time, Intra-op. fentanyl consumption, first need of analgesia, and 48 h total morphine consumption between the two groups.

	Group		
	ECI ($n = 30$)	PCI ($n = 30$)	
	Median (Range)	Median (Range)	p-value
CVP pre-operative (Cm.H2o)	8.00 (3.00–13.00)	8.00 (3.00–13.00)	0.883
CVP24 h(Cm.H2o)	9.00 (5.00–16.00)	10.00 (5.00–16.00)	0.423
CVP 48 h (Cm.H2o)	11.50 (9.00–16.00)	12.00 (9.00–16.00)	0.438
p-value over time	**<0.001***	**<0.001***	
Intra-op. fentanyl consumption (µg) median (IQR)	200.00 (100.00–250.00)	200.00 (150.00–250.00)	0.497
First need of Analgesia (h) mean±SD	8.40 ± 12.08	4.83 ± 7.76	0.252
48 h Total morphine consumption (mg) median (IQR)	7.00 (6.00–8.00)	9.00 (7.00–10.00))	**0.002***

consumption was comparable in both groups with no significance ($p = 0.497$) (Table 2).

Regarding postoperative pain severity by NRS score, both groups showed non-significant reduction at most postoperative study times, more noticed in ECI group, except for NRS 6-, 12-, and 24-hour scores where ECI group patients had a significant reduction compared to other group, At 6 h; **($p = 0.034$*)**, at 12 h; **($p = 0.015$*)**, at 24 h; **($p = 0.011$*)**, respectively (Figure 2).

The time of first analgesic request was earlier in PCI group than ECI group (ECI vs PCI), mean ±Sd; 8.40 ± 12.08 vs 4.83 ± 7.76 respectively, but without significance ($p = 0.252$) (Table 2). While 48 h total morphine consumption, presented by median, showed statistically significant reduction in patients of ECI group compared with patients of PCI group; 7.00 mg vs 9.00 mg ($p = 0.002$*) (Table 2).

Hemodynamics, heart rate and mean BP were evaluated perioperatively. Both groups were similar regarding pre- and intraoperative hemodynamics. But postoperative mean BP measures in both groups were reduced than baseline measure showing more non-significant reduction in ECI group (Table 3). Moreover, postoperative Hr. measures were non significantly reduced in both groups until 24 h, at which and then, the H.R became significantly reduced in ECI group than other group; at 24 h **($p < 0.030$*)**, at 36 h **($p < 0.001$*)**, and at 48 h **($p = 0.001$*)** respectively (Table 4).

Our study as regard Cardiac enzymes, Troponin I and BNP, showed no significant differences between the two groups at each time point. While there was a non-significant change in the troponin level over study time in both groups (Figure 3), there was a significant decrease in BNP level over study time in the ECI group ($p = 0.045$*) with non-significant decrease in the PCI group ($p = 0.078$) (Figure 4).

Regarding morphine side effects, PONV, both groups showed no significant differences, (ECI vs PCI); 8 vs 6 cases of nausea (P=0.542), 7 vs 4 cases of vomiting ($p = 0.317$) respectively (Table 5). Hypotension was significantly reported in ECI group; eight cases (26.7%) vs two cases (6.7%) in the PCI group (p= 0.038*) (Table 5). On the other side, two cases (6.7%) of hypertension were found

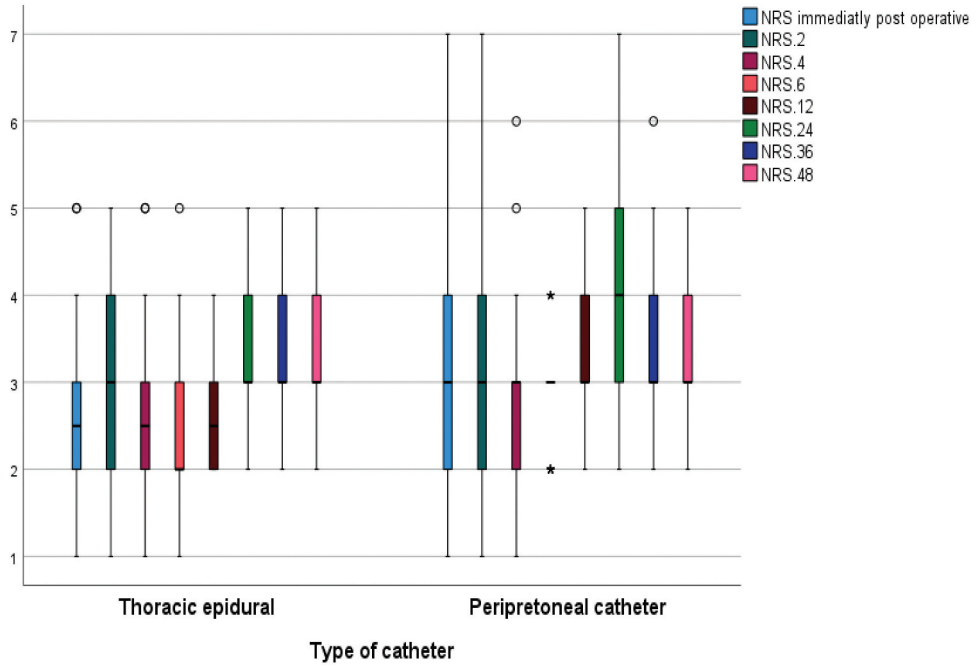

Figure 2. Postoperative NRS score over study time between two study groups.

Table 3. Perioperative mean blood pressure over study time between the two study groups.

	Groups		
	ECI ($n = 30$)	PCI ($n = 30$)	
	Mean ±SD	Mean ±SD	P-value
mean BP baseline (pre-op)	100.40 ± 11.15	100.77 ± 12.69	0.906
mean Bp 1 h (Intra-op)	82.97 ± 9.86	80.70 ± 10.84	0.400
mean Bp 2 h (Intra-op)	82.27 ± 7.06	80.30 ± 7.21	0.290
mean Bp 3 h (Intra-op)	84.87 ± 5.52	84.63 ± 5.90	0.875
mean Bp 4 h (Intra-op)	90.10 ± 4.86	89.43 ± 5.20	0.610
mean Bp 5 h (Intra-op)	95.63 ± 4.41	94.90 ± 5.03	0.551
mean BP 0 h (Immediately post-op)	77.30 ± 12.83	81.13 ± 14.85	0.219
mean BP2h	74.63 ± 13.40	82.43 ± 15.28	0.052
mean BP4h	75.20 ± 14.08	83.47 ± 16.55	0.054
mean BP6h	79.20 ± 13.37	85.43 ± 13.20	0.091
mean BP12h	83.80 ± 12.64	87.67 ± 9.70	0.099
mean BP24h	86.43 ± 11.32	88.87 ± 7.25	0.134
mean BP36h	88.27 ± 8.07	91.13 ± 7.65	0.163
mean BP48h	93.43 ± 8.20	94.03 ± 7.71	0.771

in PCI group vs one case (3.3%) in ECI group without **significant** differences ($p = 0.554$) (Table 5).

Bradycardia was reported as statistically significant by seven cases (23.3%) in ECI group versus one case in the PCI group (3.3%) ($p = 0.023$*). Moreover, two cases of dysrhythmia noticed in ECI group vs one case in PCI group ($p = 0.554$) (Table 5). No reported cases of myocardial ischemia or heart failure in both groups (Table 5).

5. Discussion

Postoperative problems are frequent, with myocardial damage being the most common [2,15], as several studies have indicated that considerable proportion of patients undergoing non-cardiac surgery suffer from unfavorable cardiovascular outcomes [16].

Based on a previous study conducted in our institute by Mohamed et al, thoracic epidural analgesia in patients undergoing major abdominal surgery reduced postoperative MACEs considerably while providing better pain control than IV analgesia [8]. Our present study validated the efficacy of preperitoneal catheter analgesia in lowering postoperative MACEs in cancer patients subjected to upper abdominal surgeries when compared with epidural catheter analgesia. The 48-hour interval for PCA was selected since most unrecognized AMI occur during the early postoperative period [17].

Numerous studies that evaluated the analgesic efficiency of preperitoneal catheters with standard epidural after abdominal surgery have revealed that CWI has offered comparable or at least not inferior results, such as a research by Mungroop et al, [18].

Although, patients of PCI had a higher significant NRS scores at some time points postoperatively (from 6- till 24hrs); at 6 h; ($p = 0.034$*), at 12 h; ($p = 0.015$*), at 24 h; ($p = 0.011$*), respectively, with higher postoperative morphine consumption than ECI patients; that showed a non-significant reduction of NRS scores at most study times, they did not reach the clinical significance. The mean cumulative NRS values were low in both groups and within the range of mild pain, and the total 48 h cumulative morphine consumption was also reduced, (ECI vs. PCI), median; 7.0 mg vs 9.0 mg, showing statistically ($p = 0.002$*) but not clinically significant reduction in ECI group.

Intraoperative fentanyl consumption and time of first analgesic demand were not significant between both groups. These findings were consistent with an earlier

Table 4. Perioperative heart rate over study time between the two study groups.

	Groups		
	ECI ($n = 30$)	PCI ($n = 30$)	
	Mean ±SD	Mean ±SD	p-value
HR baseline (Pre. Op)	90.80 ± 14.04	89.03 ± 13.10	0.616
HR 1 h (Intra. Op.)	74.20 ± 8.88	78.27 ± 11.99	0.141
HR 2 h (Intra. Op.)	77.57 ± 7.25	77.07 ± 9.89	0.824
HR 3 h (Intra. Op.)	77.70 ± 7.11	77.00 ± 8.40	0.729
HR 4 h (Intra. Op.)	79.60 ± 5.98	78.77 ± 7.31	0.631
HR 5 h (Intra. Op.)	85.53 ± 7.45	86.10 ± 8.57	0.786
HR 0 h (immediately post. Op.)	104.10 ± 11.23	105.33 ± 9.82	0.652
H.R 2 H	93.87 ± 13.42	96.60 ± 10.81	0.389
H.R 4 H	88.50 ± 9.79	91.67 ± 6.41	0.381
H.R 6 H	86.20 ± 8.38	89.53 ± 6.33	0.125
H.R 12 H	84.50 ± 7.72	85.33 ± 6.08	0.419
H.R 24 H	79.33 ± 5.78	81.50 ± 6.05	**<0.030***
H.R 36 H	85.37 ± 3.86	92.70 ± 6.68	**<0.001***
H.R 48 H	91.23 ± 6.54	95.77 ± 6.98	**0.001***

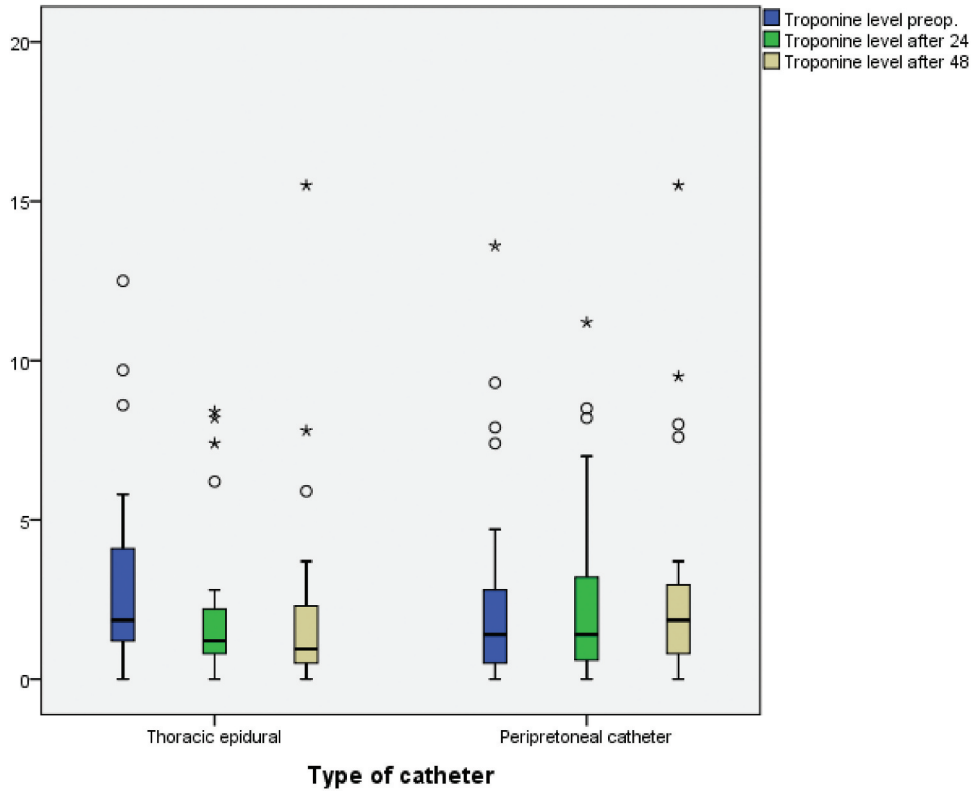

Figure 3. Box and whisker plot showing troponin distribution over study time and between two studied groups.

study by Othman et al, who concluded that preperitoneal catheter provided comparable analgesia to the epidural catheter by reducing pain intensity and total morphine consumption with its systemic side effects [19].

Contradictory to our findings, many studies suggested superior results of wound catheter analgesia [20–22], While, other studies revealed inferior results when compared to epidural analgesia [23,24]. This discrepancy with unanticipated outcomes could be explained by more severe pain of upper abdominal surgical incisions restricting patient and respiratory movements than lower abdominal, colorectal, or caesarean section incisions.

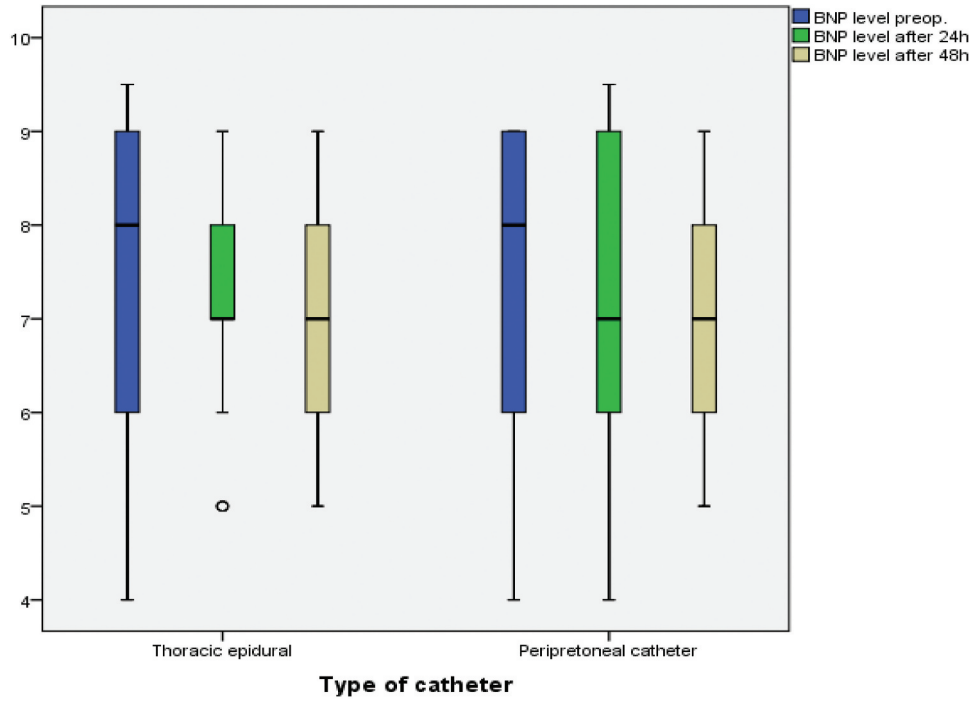

Figure 4. Box and whisker plot showing BNP distribution over study time and between two studied group.

Table 5. Postoperative side effects and cardiovascular complications between the two study groups.

	Group		
	ECI ($n = 30$) n (%)	PCI ($n = 30$) n (%)	p-value
Vomiting	7/30 (23.3%)	4/30 (13.3.0%)	0.317
Nausea	8/30 (26.7%)	6/30 (20.0%)	0.542
Hypotension	8/30 (26.7%)	2/30 (6.7%)	**0.038***
Bradycardia	7/30 (23.3%)	1/30 (3.3%)	**0.023***
Hypertension	1/30 (3.3%)	2/30 (6.7%)	0.554
Dysrhythmia (Newly diagnosed)	2/30 (6.7%)	1/30 (3.3%)	0.554
Angina	0/30	0/30	-
Myocardial injury (MI)	0/30	0/30	-
Heart failure	0/30	0/30	-

Pre- and intraoperative hemodynamic values were similar between both groups. Postoperative values showed more non-significant reduction in ECI group when compared to PCI group regarding mean blood pressure and H.R but with more significant decrease in H.R at each time point from 24 h and then in ECI group; at 24 h (***p* < 0.030***), at 36 h (***p* < 0.001***), and at 48 h (***p* = 0.001***). Also, CVP values were similar with improvement over study time. Our findings agreed with those of Elshamaa et al, who observed no significant variations in hemodynamic parameters between the two groups [25].

Recent research suggests that measuring troponin or CK-MB after surgery can predict a patient's risk (within 12 month) of severe cardiovascular events or death as suggested by Levy et al. [26]. The first 48 hours following MI carry the most risk for death. As a result, several researchers have proposed for monitoring perioperative troponin levels in noncardiac surgical patients to identify at-risk individuals [27].

A study was conducted in our institute on 60 ischemic patients who underwent major abdominal surgeries and reported that, when paired with epidural analgesia, general anesthesia offered superior pain relief, and the ischemic cardiac events were comparable in both groups [28]. Another study discovered that plasma cardiac troponin I concentrations were within normal ranges (0.1 mg/L) in all groups concluding that epidural analgesia, is preferable for high-risk cardiac patients [29].

Here, cardiac enzymes, Troponin I and BNP, values were similar without significance between both groups and within normal ranges for age group. These lab data were closely associated with clinical findings, as no occurrences of myocardial damage or heart failure were reported in either group, indicating the efficacy of the preperitoneal catheter in limiting the occurrence of MACEs.

Postoperatively, hemodynamic affection was significantly presented in ECI group with eight cases of hypotension, and seven cases of bradycardia, compared to two cases of hypotension and one case of bradycardia in PCI group (***p*=** 0.038* & 0.023* respectively). On the other side, two cases of hypertension were found in PCI group (6.7%) vs 1 case (3.3%) in ECI group without **significant** differences ($p = 0.554$). Moreover, non-fatal dysrhythmia, without hemodynamic affection and recovered by removal of continuous epidural infusion then dose reduction, was noticed as two cases in ECI group vs 1 case in PCI group without significance ($p = 0.554$). So, our study demonstrated that, while preperitoneal analgesia did not provide a superior alternative to epidural analgesia, it did provide comparable hemodynamics.

Morphine side effects, PONV, were non-significant between groups, explained by approximate amounts of total morphine consumption in both groups. I.v 8 mg of ondansetron was used to cure PONV, and if that didn't work, 10 mg of metoclopramide was used. Our results were comparable with a study by Bertoglio reported that the CWI group had a decreased incidence of PONV due to the quick return of bowel function [20].

Within 48 h follow-up period, no significant pulmonary or cardiovascular problems occurred and no further epidural block complications were detected in both groups.

6. Study limitations and future studies

Our patients were non-cardiac, ASA I or II, patients without serious underlying diseases. Multiple surgical incisions with variable catheter placement. High cost and availability of the preperitoneal catheter were a strong limitation.

7. Conclusion

PCI of levobupivacaine in major upper abdominal cancer surgeries has a good analgesic, cardioprotective and hemodynamic effects comparable to the epidural analgesia but with less side effects; hypotension, bradycardia and PONV, beside its use when epidural analgesia is not desired or forbidden.

Abbreviation

PCI= preperitoneal catheter infusion, ECI=epidural catheter infusion, NRS=numerical rating scale, PONV= postoperative nausea and vomiting, PMI= perioperative myocardial infarction, MINS= Myocardial injury after noncardiac surgery.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Availability of data and materials

The original contributions presented in the study are included in the article and further inquiries can be directed to the corresponding author.

Ethics Committee Approval

Ethical committee approval was received from south Egypt cancer institute Review board (IRB).

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