

# Pain Management After Pancreatic Resections for Cancer

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## Abstract

**Introduction:** Pancreatic cancer is being known for his aggressiveness and surgical resection is the only potentially curative treatment. Effective analgesia in pancreatic surgery is required for early recovery and healing.

**Methodology:** We have undertaken a retrospective study on 81 patients who underwent pancreatic resections for pancreatic cancer over 5 years with intravenous and epidural perioperative analgesia.

**Results:** Sixty-two patients with pancreatoduodenectomy and 19 patients with distal pancreatectomy for malignant tumors, aged 31 to 79 years were included. The epidural analgesia was applied mostly for pancreatoduodenectomy (33 patients) and only in 1 patient with distal pancreatectomy. The median operative time was similar for patients with intravenous analgesia and those with epidural. There was no statistically significant difference in the incidence of postoperative complications between the two groups, but epidural analgesia was associated with a longer stay in intensive care unit (median 5 days vs 4 days,  $p=0.141$ ).

**Conclusions:** Both intravenous and epidural analgesia provide a successful pain control in the immediate postoperative period, with no significant difference concerning the rate of postoperative complications.

## Introduction

Pancreatic cancer is the seventh leading cause of cancer mortality in industrialized countries, being known for its aggressiveness and poor prognosis [1]. Surgical resection is the only potentially curative therapy for pancreatic cancer. Epidemiological data indicate that only 20% of patients with early-stage disease are suitable for radical surgical resection [2]. Pancreatoduodenectomy (PD) is considered to be the only curative treatment for malignant lesions of the pancreatic head region [3]. Since first described by Whipple et al., despite multiple technical improvements and variants, the morbidity of PD remains as high as 40% [4,5]. Distal

pancreatectomy is indicated for tumours of the body and tail of the pancreas and usually requires spleen removal along with the tail of the pancreas, because of the close proximity between the two organs and the necessity of proper lymphadenectomy [6,7]. Postoperative pain is the most feared symptom for most patients and its management might be difficult [8]. Effective analgesia after pancreatic surgery is required for early mobilisation, optimal respiratory function, and prevention of thromboembolic complications [9]. Epidural analgesia is often use for intraoperative and postoperative pain management in pancreatic surgery. This

procedure is associated with effective postoperative analgesia, decreasing in pulmonary or cardiac complications, earlier restart of gut motility and a cutback in thromboembolic complications [9,10]. The continuous local analgesia by wound infiltration was reported as a pain management procedure as effective as epidural analgesia [10]. As an alternative, opioids-based analgesia is the most frequently used [9,11].

## Materials and Method

Eighty-one pancreatic resections for pancreatic cancer, performed at the Surgical Clinic 2, "St.Spiridon" Emergency Hospital from Iasi, Romania, from January 2014 to December 2018 were included in this study. A database was created with all patient characteristics, including demographic data, clinical data, laboratory data, imaging data (diagnosis and follow-up), surgical protocols, histopathological reports, and postoperative data, including analgesia. Patients with perioperative and postoperative thoracic epidural analgesia were identified and two groups were created: A = patients with intravenous analgesia alone; B = patients with epidural analgesia. The two groups were matched in terms of demographic data.

## Results

Eighty-one patients with radical pancreatic resections for malignant tumours were included in this study, aged 31 to 79 years (mean age: 61.5 years). PD was performed in 62 patients and distal pancreatectomy in 19 patients, under general anaesthesia. During PD, the pancreato-jejunal anastomosis was reconstructed as an end-to-side duct-to-mucosa protected with a catheter anastomosis or a two-layer pancreato-jejunal anastomosis. Patient characteristics and tumor features were presented in Table 1. Before surgery, 34 patients were initially submitted to thoracic epidural analgesia placed within a T7-T9 interspace level according to standard procedures. A continuous epidural infusion was initiated 20 min before surgical incision and consisted of bupivacaine 0.1% 1 mg/ml, continued during the surgical procedure, and up to 4 days postoperatively.

The epidural analgesia was applied mostly for PD (33 patients) and only in 1 patient with distal pancreatectomy. The median operative time was similar for patients with intravenous analgesia and those with epidural. There was no statistically significant difference in the incidence of postoperative complications between the two groups, but epidural analgesia was associated with a longer stay in intensive care unit (median 5 days vs 4 days,  $p=0.141$ ) (Table 2).

In our group study, non-steroidal anti-inflammatory drugs are the first-line agents most used for the control of mild pain in postoperative recovery time (Table 3). The switch to another class of pain control drugs was made after the assessment of the dosage at regular time intervals. Strong opioids were used only in intensive

care unit for patients with moderate and severe pain with no response at non-opioids.

**Table 1:** Patient characteristics and tumor features.

Mean age (SD), years	61.5
Males, n (%)	49 (60.49)
<b>ASA classification n (%)</b>	
I	11 (13.58)
II	51 (62.96)
III-IV	19 (23.45)
<b>Co-morbidity, n (%)</b>	
Cardiac	24 (29.62)
Hypertension	35 (43.20)
Pulmonary	1 (1.23)
Diabetes mellitus	22 (27.16)
<b>Surgical procedures, n (%)</b>	
Whipple pancreaticoduodenectomy	52 (64.21)
Pylorus preserving pancreaticoduodenectomy	10 (12.34)
Distal pancreatectomy	19 (23.45)
Operation time (min)	185.8 +/-31.6
Blood loss (ml)	225.6 +/-104.3
Intensive care unit stay (days)	5.3 +/-0.9
Hospitalization (days)	15.52 +/-9.01
<b>Perioperative analgesia, n (%)</b>	
Exclusive Intravenous	47 (58.03)
Epidural	34 (41.97)
<b>Tumour stage, n (%)</b>	
Ø T1	7 (8.65)
Ø T2	24 (29.62)
Ø T3	45 (55.55)
Ø T4	5 (6.18)
<b>Tumour location, n (%)</b>	
Ø Head	57(70.38)
Ø Body	5(6.17)
Ø Tail	19(23.45)
<b>Tumour invasion, n (%)</b>	
Ø Lympho-vascular	39 (48.14)
Ø Perineural	64(79.01)

**Table 2:** Postoperative complications.

	A. Intravenous (N=47)	B. Epidural (N=34)	p
No complications	25	11	0.498
Pancreatic fistula	6	5	0.0418
Delayed gastric emptying	4	7	0.316
Pancreatitis	8	1	0.053
Biliary leak	3	2	0.218
Digestive leakage	2	0	0.156
Hemoperitoneum	3	2	0.3
Intraperitoneal abscess	3	3	0.242
Wound infection	4	3	0.418
Mortality	6	3	0.347

**Table 3:** Intravenous analgesia

Intravenous analgesia	Perioperative (%)	Postoperative (%)
Non-opioid: Paracetamol, Diclofenac	3.75	48.75
Intermediate opioid: Tramadol	18.75	36.25
Strong opioid: Morphine, Fentanyl, Methadone	77.5	15

## Discussion

Pancreatic resections are major surgical abdominal procedures, associated with high morbidity rate. There is a correlation between inflammation and cancer development and recurrence, as well as between the postoperative inflammatory response and the development of persistent pain syndromes [12]. Epidural analgesia can mitigate the inflammatory response by creating a sympathetic blockade [13]. Besides its role as an effective tool for anesthesiologists in acute pain management, there are studies suggesting that epidural analgesia decreases the postoperative morbidity in pancreatic surgery, reducing the incidence of cardiovascular, respiratory and thromboembolic complications or ileus [14,15]. In the early postoperative period, the use of epidural analgesia can also improve patient recovery. By producing a sympathectomy, it allows the dominance of the parasympathetic system, thus accelerating the return of gut motility [16]. This benefit of epidural analgesia is particularly valuable for one of the most common complication after PD, delayed gastric emptying [17].

The use of the thoracic epidural analgesia increased in the last 10 years in our department but is still not included in the routine protocol for major surgery. Our study found no significant difference concerning the complications rate for the patients with epidural analgesia and intravenous analgesia. Similar results regarding gastrointestinal complications after pancreatic resections were found by a randomized clinical trial recently published [18]. In our

group with epidural analgesia, a better pain control was achieved in the immediate postoperative time. Intensive unit care stay was longer, but with no impact on the hospitalization period. The period of postoperative pain control obtained by epidural analgesia compared to intravenous analgesia was highly discussed and a randomized trial revealed a better pain management with epidural analgesia in the first 48 hours after hepato-pancreato-biliary surgery [18,19]. Concern is raised by the hemodynamic instability associated with pancreatic surgery. It can occur independently of the type of analgesia, but also as a side effect of epidural analgesia, prompting the closure of the epidural infusion [20].

Also, the necessity of fluid resuscitation increases the risk of pulmonary or bowel wall oedema and may contribute to a higher incidence of pancreato-jejunal anastomotic leakage and subsequent pancreatic fistula [21]. Several prospective, single blind, randomized control trials are still investigating the benefits of epidural analgesia in pancreatic resections, including patient recovery and healing, serum inflammatory markers, and tumour recurrence and overall survival [22]. Limitations of this research are its retrospective design, the fact that is a single centre study, with small sample size and an uneven number of procedures between the two groups.

## Conclusion

Even if an improvement of the long-term outcome after pancreatic surgery was not correlated with the type of peri- and postoperative analgesia, both intravenous and epidural analgesia provide a successful pain control in the immediate postoperative period. The choice between intravenous and epidural analgesia is based on complex clinical and biological pre-operative assessment, both procedures being effective and safe for postoperative pain management.

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