

Study Title: Implementation of a pain management plan in major open abdominal surgeries.

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Ο ΕΥΑΓΓΕΛΙΣΜΟΣ

1.Abstract

Major abdominal surgery encompasses a broad range of surgical procedures in heterogenous patient populations.Management of postoperative pain has received keen attention in recent years with considerable concurrent advancement in the field.Despite this improvement,postoperative pain continues to be a challenge since suboptimal postoperative pain control is a risk factor for persistent surgical pain,increased morbidity,poorer functional recovery and reduced quality of life. Therefore,analgesic strategies should regard patients' factors as well as surgical procedures peculiarities.Since efforts are made throughout the years and are of utmost importance as numerous analgesic options exist for the effective pain control after abdominal surgeries including multiple classes of drugs and routes of administration(i.e.parenteral,regional,neuraxia.) Within the broad category of major abdominal surgery,upper gastrointestinal surgery is frequently associated with the greatest surgical insult and resultant higher intensity of postoperative pain.For example,a recent systemic review of epidural analgesia in patients undergoing pancreatoduodenectomy in 2019,among a large number of patients,the reported results show lower postoperative pain scores,lower complication rates,decreased hospital length of stay as well as mortality.[22]

In the context of the current surgical environment where improvement has been made,emphasis is placed on precision,minimizing trauma and improving the outcome.The choice of postoperative pain analgesic modality,is at the discretion of the primary anaesthesiologist and the choice depends upon the plan favored by him/her as well as the availability of drugs and equipment. Continuous re-evaluation of analgesic strategies is a necessary step toward establishing a better pain management plan in major abdominal surgeries and to design guidelines to improve our clinical approach.

1A.Patient selection criteria:

A demanding factor in the ultimate fulfillment of this operation and cure, is proper selection of candidates,requiring a thorough evaluation for the presence of metastasis,confirming any disease beyond TME(Total mesorectal excision)requiring multivisceral or pelvic excision.A chest X-ray and computed tomographic (CT) scan of the pelvis and abdomen are the minimal tests necessary for the evaluation. The CT scan provides evaluation of the liver, retroperitoneal lymph nodes, and urinary tract and allows better evaluation of sidewall involvement by the tumor in the pelvis.Loss of tissue planes in the lateral pelvis indicates

invasion of the tumor into the pelvic musculature.[4]

The absolute and relative contraindications to open abdominal surgeries vary.A study by Huang and colleagues regarding pelvic exenteration surgeries,describe that duration of surgery,blood loss,length of hospital stay and complication rates did not increase with age.Advanced age has been considered a relative contraindication to exenterative surgery,probably because older patients are more likely to have pre-existing medical conditions,eg:heart disease,COPD,decreased renal function and altered immunologic response.Advanced chronological age should not be considered a contraindication to potentially curative surgical procedure.[5][18]

1B.Preoperative assessment:

The aims of preoperative assessment should be determining the level of surgical fitness,ascertaining functional reserve and the ability to withstand periods of significant physiological stress,the identification of issues that can potentially result in adverse surgical and anaesthetic outcomes.Given the inherent risk involved in surgical procedure,appropriate anaesthetist-led assessment and management of various co-morbid conditions in the perioperative period,at least 1 week before the arranged date of the surgery,can considerably improve patient safety,especially among high risk patients.Generally,the high risk patients have medical comorbidities,eg:ischemic heart disease,heart failure,valvular heart disease,cardiac implantable electronic device,pulmonary disease,and diabetes mellitus.It has been suggested,that are defined as high risk patients,those with mortality risk greater than 5% and those undergoing a procedure carrying a mortality risk of >5%.[6]Over the years,anaesthetist work extended,to assessing the risk of anaesthesia,optimizing comorbid conditions,selecting patients who may benefit from additional regional techniques and identifying potential difficulties that may be encountered during operation as well as postoperative period.Cardiopulmonary exercise test(CPET),gives an integrated objective measure of functional capacity which in turn is a strong predictor of postoperative morbidity and mortality[7].Thus,determining the functional capacity is a mandatory step in preoperative assessment and is measured in METS(metabolic equivalent of tasks,goal:>4).

Additionally,the revised cardiac index,is the most approved system,since cardiovascular complications are one of the leading cause of postoperative mortality and morbidity.[8]Optimisation of lung function helps in reducing complications. Patients are advised to stop smoking for a period of 4–6 weeks,aiming in reduction of airway reactivity, improve mucociliary function and decrease carboxy-haemoglobin. The widely used incentive spirometry may be useful only when combined with other respiratory muscle exercises.

Pharmacotherapy of asthma and chronic obstructive pulmonary disease must be optimised before considering the patient for elective surgery. Beta 2 agonists, inhaled corticosteroids and systemic corticosteroids, are the main drugs used for this.Also,the ARISCAT score can be included in the preoperative assessment ,in order to predict risk of pulmonary complications after surgery.[9][10]

1C.Perioperative Management:

Considering the nature of the surgeries and its duration,general anaesthesia is compulsory.Selection of the most suitable haemodynamic and respiratory intraoperative methods,and appropriate assimilation of these,may help apprehend its status and avoid over resuscitation.[11]
Antibiotic prophylaxis should cover both aerobic and anaerobic bacteria,based on the patient's allergy status.
Furthermore,hypothermia should be prevented,using various warming systems,which in turn can result in coagulopathy,immune function suppression,cardiac and infective complications.Pressure-related neuropathy,especially among patients undergone chemoradiotherapy,can be a consequence of the nerve subjected to stretch,compression,ischaemia,trauma or a combination of these factors.[12]
Expecting possible massive haemorrhage,presents one more challenge to the anaesthetist.Due to this possibility,blood products must be ready for immediate use.[13]

1D.Pain management:

Last,but the most important pain must be considered.Cancer related pain,is a common symptom and an unavoidable outcome of cancer which affects the quality of life and the postoperative survival.Cancer patients,experience pain due to disease progression and/or treatment(chemotherapy-radiotherapy)Thus,pain management process should start from the preoperative assessment aiming in its optimization during intraoperative and postoperative period.Apart from the interpersonal differences in pain experience,the pain intensity varies based on the different surgical approach,size of incisions,type of surgery(+bone resection) and reconstructive procedure performed.Epidural analgesia,remains the cornerstone of postoperative pain control,[14] [15]Moreover,there are many published benefits including decrease of the surgical stress response,in particular neuroendocrine(sympathetic and pituitary)and metabolic(hyperglycemia and protein catabolism)effects,reduced pulmonary complications(hypoxia,atelectasis,thromboembolism)and some

evidence of reduced incidence of myocardial infarction and acute kidney injury.Additionally,epidural analgesia reduces both opioid consumption and it has been shown that maintains the immune functions of patients and is associated with a decrease in tumor recurrence. It has also been shown to reduce hypercoagulability,increases exercise capacity and accelerates the return of intestinal functions to normal. In line with this information in colorectal surgery specifically ERAS guidelines advocate the use of epidural.[16][17]In addition,multimodal analgesia has become popular through the years and in a sense,is a way of intervening to prevent pain from being experienced or reducing the pain felt to a level accepted by the patients.However,the is no conclusive evidence to support opioid avoidance with the goal to minimize the risk of cancer recurrence.[15]

2.Target

The target of the study is to compare the outcome of the selected analgesic combination of local anaesthetic and opioid(ropivacaine+fentanyl or ropivacaine +morphine)for postoperative continuous infusion,aiming to relief successfully the pain,on patients undergoing major abdominal surgeries based on hemodynamic,clinical and questionnaire findings.All patients included will receive the same:

- ☐ preoperative pain assessment -using VRS scale-
- ☐ method of central neuraxial block -epidural-
- ☐ size of Tuohy needle
- ☐ level of epidural catheter placement based on nature of the surgery(thoracic or lumbar region)
- ☐ plan of anaesthesia -General anaesthesia(Desflurane) + remifentanil
- ☐ quantity of intravenous opioids intraoperatively -remifentanil,fentanyl,morphine-
- ☐ local anaesthetic solution-ropivacaine 200ml/400mg-

The study is a prospective,comparative of two analgesic options.We will study 58 patients,equally divided into two groups, aged 18-80 years,administered to the hospital for elective open abdominal surgeries.

In group A(p:29),we will administer for postoperative pain relief - Ropivacaine 200 ml/400 mg + Fentanyl for

continuous epidural infusion for the first 5 days.The infusion will start 2 hours before the end of the operation and before the admission to the intensive care unit.

In group B(p:29),we will administer for postoperative pain relief Ropivacaine 200ml/400mg + Morphine for continuous epidural infusion for the first 5 days.The infusion will start 2 hours before the end of the operation and before the admission to the intensive care unit.

The study aims to highlight the positive impact of the chosen analgesic combination during the intraoperative period,the postoperative recovery period and also during the follow up periods in terms of physical function,pain intensity during activity,adverse effects and self efficacy.More than that,the key is to minimise the side effects of the method chosen and to achieve early mobilization.

Historically, epidural analgesia has the strongest evidence base for open abdominal surgery. They have been well studied for over 20 years and provide excellent static and dynamic analgesia provided they work.There are many published benefits many mentioned above.However, epidural analgesia is not without its own setbacks and these have been garnering increasing attention that potentially challenges the view that they are the gold standard for open abdominal surgery. Epidural failure for whatever reason (incorrect primary placement, secondary catheter migration and suboptimal dosing) is one of the most common complications and has been quoted as occurring in 27–32% of cases. Hypotension and motor block may lead to excessive intravenous fluid administration and impaired mobilisation respectively. There is a significantly increased risk of pruritus and urinary retention while,more serious rare complications include epidural haematoma and abscess formation.The current available evidence tends to highlight more benefits than risks.[21]

Study Title	**Implementation of a pain management plan in major abdominal surgeries**
Study Design	**Comparative,prospective study**
Participants	**Patients undergoing major open abdominal surgeries including pelvic exenterations,Whipple,gastrectomies,colectomies,nephrectomies,esophagectomies.**
Planned sample size	**58 patients**
Planned study period	**2025-**

2A.Objectives

Primary

- Epidural continuous infusion combination(ropivacaine +fentanyl or morphine) potent pain control using VRS scale (>4 considered as poor analgesic outcome.)

Secondary

- Preoperative Analgesia
- Intraoperative Analgesia
- Hypotensive episodes
- Vasopresor use
- Fluid Resuscitation
- Duration of surgery
- Postoperative pain intensity during 5 first days during rest&cough
- Additional analgesic admin.
- Desaturation Episodes Sp02<94%
- Nausea/Vomiting episodes
- Mobilization time
- Bower recovery time
- ICU length of stay
- Hospital length of stay

3.Methodology

The study is prospective,comparative aiming to identify the pain management agents that will provide the best postoperative relief in order to be established and used as a primary choice to patients undergoing major open

abdominal surgeries .All patients included will receive the same analgesic technique(epidural)chosen preoperatively by the anaesthesiologist in charge.All study participants are informed in detail and written informed consent is obtained.The study is in accordance with the regulations of the Declaration of Helsinki on human studies and the Greek legislation regarding personal data.

3A.Inclusion

☐ Elective surgical patients admitted to ‘’Evangelismos General Hospital’’ for open abdominal surgeries.

3B.Exclusion

Surgical patients will be excluded if they have:

☐ Coagulation disorders.

☐ Demyelinating disorders of the CNS.

☐ Severe hemodynamic instability requiring vasopressors from the early beginning of the surgery.

☐ Reported allergic reaction to local anaesthetics.

☐ Objection to take part.

3C.Parameters

☐ Patients Demographics

➔ Age

➔ Gender

➔ Ethnicity

➔ BMI calculation

➔ ASA

☐ Medical History

➔ Operations and any reported complications

➔ Comorbidities(i.e.Cardiovascular/Respiratory)

- ➔ Medications
- ➔ Smoking
- ➔ GERD
- ➔ Chemotherapy/Radiotherapy (number of cycles and last cycle)
- ☐ Pain score during preoperative assessment
    - ➔ NRS score

Preoperative,intraoperative and postoperative data are collected .Preoperatively,a clinical examination is performed and the laboratory findings are gathered.Based on preoperative medical examination any further examinations may be requested.

Intraoperatively,the following parameters will be continuous recorder:

1. Hemodynamic parameters (i.e. heart rate,mean arterial pressure,SpO2,CO,CI,SVV,HPI,BIS,CVP)before induction,immediately after induction,during the first 6-7h and during the end of the process.
2. Quantitative measurement of the administered anaesthetics,opioids,fluids,vasopressors and inotropic drugs.
3. Intraoperative complications (i.e. bleeding,hypotension).
4. Duration of the surgery.

Postoperatively,the following data will be recorded:

1. Postoperative pain will be recorded during the first 5 days after surgery,using the **NRS scale** (0-no pain/10-severe pain)in rest and during cough.Considered to have the expected good pain relief will report mean pain score during the first 72 hours between 0-4,graded as fair pain relief in patients with a mean pain score between 4,and as poor pain relief a mean pain score between 5-10.
2. Additional pain medications required.
3. Episodes of desaturation SpO2 <94%.
4. Postoperative nausea & vomiting.

5. Time required until mobilization.
6. Time required for intestinal function.
7. ICU length of stay.
8. Complications.
9. QoR-4(quality of recovery),2 weeks and 2 months postoperative.
10. Total hospital length of stay.

Power analysis determination is described below:

Exact - Proportions: Inequality, two independent groups (Fisher's exact test)
Options: Exact distribution
Analysis: A priori: Compute required sample size
Input: Tail(s) = Two
Proportion p1 = 0.1
Proportion p2 = 0.45
α err prob = 0.05
Power (1-β err prob) = 0.80
Allocation ratio N2/N1 = 1
Output: Sample size group 1 = 29
Sample size group 2 = 29
Total sample size = 58
Actual power = 0.8106139

4.Expected Results

Our study inquires into the choice of the best analgesic technique and medication combination in order to relieve pain related to cancer.Epidural technique, is a reliable method which will provide the most effective pain minimization,hemodynamic stability and reduction of intraoperative and postoperative complications.Moreover,postoperative pain relief ,besides being humanitarian,aims to improve patient's psychological,cardiovascular as well as respiratory function.The awareness of all the above is first in order of importance,for anesthesiologists and specialists involved in this particular type of surgery.Predicted cancer mortality rates remain favorable in the EU and UK and attention should be pain to the predicted increases in CRC mortality in young adults.Specifically,pelvic exenterations are newly

introduced in Greece but they are evolving constantly world widely i.e.England,Australia. since the first surgery in 1948.And while,epidural technique is proposed to these patients,taking into account the detailed knowledge of all the factors we can provide pain control while minimizing the side effects.

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ΓΕΝΙΚΟ ΝΟΣΟΚΟΜΕΙΟ ΑΘΗΝΩΝ
Ο ΕΥΑΓΓΕΛΙΣΜΟΣ