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Pain management in ERAS® approach for abdominal surgery: A narrative review

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. *ABSTRACT.* Tra tutte le fasi dell'intervento chirurgico, la fase preoperatoria è generalmente vissuta dal paziente con maggiore ansia. Studi in merito dimostrano che una maggiore percezione dell'ansia o paura nella fase preoperatoria sia scientificamente correlata a un decorso postoperatorio prolungato. Il dolore è annoverato tra le principali cause che recano ansia al paziente. L'obiettivo della presente revisione della letteratura è quello di esaminare la letteratura in merito alla gestione del dolore preoperatorio nei pazienti candidati alla chirurgia addominale, confrontando gli outcome clinici dei pazienti sottoposti a metodologia ERAS[®] con quelli ottenuti con una gestione perioperatoria tradizionale. Gli studi hanno dimostrato che l'analgesia perioperatoria è più efficace con il protocollo ERAS[®] rispetto ai trattamenti tradizionali. L'elemento chiave del protocollo ERAS[®] è la minimizzazione dello stress psicofisico legato all'intervento chirurgico, attraverso un approccio multimodale e multidisciplinare.

s SUMMARY. Greater fear or distress prior to surgery is associated with a slower and more complicated postoperative recovery. The main objective of this study is to examine the best evidence of the perioperative pain management in patients candidated for abdominal surgery comparing the clinical outcomes achieved with the ERAS[®] protocol to those achieved with traditional perioperative management. The studies showed that perioperative analgesia was more effective with ERAS[®] protocol than with traditional treatments. The key element of the ERAS[®] protocol is to minimize the psychophysical stress related to the surgical intervention, through a multimodal and multidisciplinary approach.

Keywords: Pain, Multimodal management, Abdominal surgery

INTRODUCTION

Greater fear or distress prior to surgery is associated with a slower and more complicated postoperative recovery (Egbert, Battit, Welch & Barlett, 1964; Kiecolt-Glaser, Page, Marucha, MacCallum & Glaser, 1998). The *Enhanced Recovery After Surgery* (ERAS*) protocol was developed to achieve early recovery after surgical procedures. The key elements of ERAS* protocol are preoperative counselling, optimization of nutrition, standardized multimodal analgesic and anesthetic regimens and early mobilization.

The history of Enhances Recovery After Surgery (ERAS®)

The new term Enhanced Recovery After Surgery (ERAS) derives from the expression "improved recovery after surgery" which initially identified a philosophy of advanced management of the patient undergoing colorectal resective surgery and that aimed to optimize the perioperative path as already proposed by Kehlet (1997). In fact, Kehlet (1997) recommended a model to provide new standards of care and to improve clinical and care outcomes. These programs attempt to modify the physiological and psychological responses to major surgery (Fearon et al., 2005). In addition, ERAS® protocol can lead to a reduction of complications and hospital stay as well as to an earlier resumption of normal activities. Several single-center and multicenter studies, as well as a systematic review (Carmichael et al., 2017) affirmed that the benefit of ERAS® protocol is to significantly improving quality of life and psychosocial adjustment, reducing hospital length of stay, and reducing hospital costs also in other types of surgery. Various studies reported interesting results about this multimodal and multidisciplinary approach. For example, in a recent study, the postoperative hospitalization time was only 48 hours. Moreover, in the first two days after surgery, a significant number of patients, mobilized every 5 hours and started a fluid diet (2000 ml), had normal intestinal functions, reported a low intensity of pain and showed no medical or surgical complications in the following thirty days (Teixeira et al., 2018).

This model was the result of the most innovative anesthesiology techniques acquisition (see Table 1), the development of minimally invasive surgical techniques and the spread of evidence-based medicine and nursing (Dionigi, 2016; Kehlet & Mogensen, 1999).

In addition, the ERAS^{*} protocol was developed from the results of the Fast Track model. The main objectives of the Fast Track protocol are early return to normal gastrointestinal functions, pain control, mobilization and reduction of complications, rational use of anesthesia techniques and analgesic measures, optimal perioperative management, choice of the best surgical technique and nutritional support modalities (Di Muzio et al., 2019). This translates into a significant reduction in postoperative complications, early mobilization, and in a reduction of the paralytic ileus, which permits a better recovery of the solid diet and an earlier return to normal intestinal function (Dionigi, 2016).

ERAS® in different surgical disciplines

Successful implementation of ERAS[®] pathway across the spectrum of surgical care could have a great impact on both patient outcomes and healthcare delivery systems. Initially, the ERAS[®] protocol has been developed for colorectal surgery, where it is considered as the best care. Several RCTs and metaanalyses showed that the introduction of ERAS[®] protocol to colorectal surgery decreased postoperative morbidity by 40-50% (Greco et al., 2014). In addition, a Cochrane review in colorectal surgery showed a reduction in length of stay and complication rates (Spanjersberg, Reurings, Keus & van Laarhoven, 2011).

Another meta-analysis (Yu et al., 2014) also showed the effectiveness of ERAS[®] pathway in the gastric surgeries, with a significant decrease in postoperative hospital stay.

Similar results have been reported in the ERAS* protocol implementation across the liver and pancreatic surgery. In fact, this protocol has a positive impact on perioperative care and it reduces operative risk (Lassen et al., 2012). Little is still known about the ERAS* pathway implementation for patients with cancer (Pędziwiatr et al., 2017).

What is ERAS®?

The ERAS[®] protocol is a multimodal program of interventions, divided into pre, intra and postoperative phases, with a multidisciplinary and integrated approach, designed to minimize metabolic stress and postoperative

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Table 1 - Descriptions of various analgesic technique

Thoracic Epidural Analgesia (TEA)	This technique consists of inserting an epidural catheter in position T6-T8 for surgery in the upper abdominal regions, and in position T9-T11 for surgery in the lower abdominal quadrants.
Spinal analgesia	It has been shown that a single dose of local spinal anesthetic in combination with intrathecal administration of morphine or diamorphine is effective in reducing postoperative recovery time in patients treated with laparoscopic surgery (Levy, Scott, Fawcett, Fry & Rockall, 2011). In addition, the use of spinal analgesia in combination with intrathecal opioid is efficient in reducing systemic opioid demand in postoperative patients, improving analgesia (Wongyingsinn et al., 2012).
Abdominal wall blocks	Abdominal wall blocks, and in particular the blocks of the transverse plane of the abdomen (TAP-Block), consist of the infiltration of local anesthetics into the neurovascular plane located between the internal and transverse oblique muscles of the abdomen.
Intravenous lidocaine infusion	It is used as an adjuvant in systemic opioid therapy and lead to a better postoperative analgesia with a reduction in opioid consumption in postoperative, and an early postoperative recovery in particular for the gastrointestinal function (Carlisle & Stevenson, 2006).
Continuous infiltration of the surgical wound	This procedure consists of an infiltration of local anesthetics in the abdominal wound, after open surgery, and improves postoperative analgesia as well as reduces opioid consumption after surgery (Mendonça, Reis, Aguiar & Calvano, 2015).
Intraperitoneal administration of local anesthetics	Intraperitoneal nebulization of ropivacaine allows a more homogeneous distribution of the anesthetic in the abdomen and it is therefore more effective (Kahokehr, Sammour, Srinivasa & Hill, 2011).

organ dysfunctions and bring the patient back to autonomy in the shortest possible time (Di Muzio, 2014). The ERAS^{*} protocol has different items to be performed during the patient surgical path, such as preoperative information and education, carbohydrate drink administration, both the evening before and the morning of the day of surgery, to reduce hunger and thirst, preoperative anxiety and postoperative insulin resistance (Di Muzio, 2014).

The success of a surgical procedure requires a multidisciplinary team approach (Chiarini et al., 2017; Di Muzio, Marinucci, De Benedictis & Tartaglini, 2017). Surgeons, anesthetists, nurses, dieticians, physiotherapists and psychologists, as members of the same surgical team, should be encouraged to consider themselves responsible at the same level of both the patient and the outcome, despite the need to have a project manager, who has the overall responsibility to plan, monitor and control all the phases of the project. Education and management of expectations, patient empowerment, psychological preparation for surgery increase coping strategies and improve the capacity to manage anxiety, one of the main risk factors for the onset of pain in postoperative care (Ayyadhah Alanazi, 2014). The fundamental point, in pain management (Sturgeon, 2014), is to implement alternative forms of pain control (see Table 2), rather than the traditional use of opioids. Table 2 – Descriptions of psychological therapies for pain

Cognitive-behavioral therapy (CBT)	This approach applies biopsychosocial approach to pain that targets behavioral and cognitive responses to pain. It involves psychoeducation about pain, behavior, mood, strategies for relaxation, behavioral activation, positive event scheduling, effective communication, and cognitive restructuring for distorted and maladaptive thoughts about pain.
Mindfulness-based stress reduction	It promotes a nonjudgmental approach to pain and uncoupling of physical and psychological aspects of pain; teaches "nonstriving" responses to pain through experiential meditations and daily mindfulness practice intended to increase awareness of the body and proprioceptive signals, awareness of the breath, and development of mindful activities.
Acceptance and commitment therapy	It focuses on development of acceptance of mental events and pain and ceasing of maladaptive attempts to eliminate and control pain through avoidance and other problematic behaviors; emphasizes awareness, defusion, and acceptance of thoughts and emotions as well as behavioral engagement in pursuit of personal goals.
Operant-behavioral therapy	It focuses on extinguishing maladaptive behavioral responses and fostering of adaptive behavioral responses to pain. Behavioral responses are altered through reinforcement and punishment contingencies and extinction of associations between threat value of pain and physical behavior.

METHODS

A narrative review was conducted to examine the best evidence of the perioperative pain management in patients candidates for abdominal surgery comparing the clinical outcomes achieved with the ERAS* protocol to those achieved with traditional perioperative management.

To search the databases, the clinical research question was formulated according the Population and their problem, Intervention, Comparison, Outcomes and Methodology (PICOM) approach. The Population included adult patient with postoperative pain after abdominal surgery. The Intervention was the ERAS[®] pathway implementation, while the Comparison was the traditional management of postoperative in abdominal surgery. The Outcomes were a reduction of the intensity and a reduction of postoperative hospital stay. The PICOM method is shown in Table 3.

The "Enhanced Recovery After Surgery AND Abdominal Pain" search string was used to query several databases such

as PsycINFO, Cochrane Database of Systematic Re-view, PubMed, CINAHL, in June and July 2019. This research identified 106 articles that were subjected to further screening for relevance of the study to the question, design of the study, type of intervention, data analysis and clinical relevance. At the end of the screening process, 8 studies were considered as most relevant for this review (see Figure 1).

Inclusion and exclusion criteria for the study were the following:

Inclusion criteria:

- studies of the ERAS[®] protocol's pain management techniques for abdominal surgery, including metaanalyses, systematic reviews, randomized clinical trials and retrospective studies;
- studies published in the last ten years, in Italian and English.

Exclusion criteria:

 studies examining gynecological, urological and aesthetic abdominal surgery and those not yet completed.

P (Population/Patient)	Adult patient with postoperative pain after abdominal surgery
I (Intervention)	Enhanced Recovery After Surgery Protocol
C (Comparison)	Traditional management of postoperative pain in abdominal surgery
O (Outcome)	Reduction of the intensity and duration of pain
M (Methodology)	RcT's, meta-analysis; systematic reviews; randomized and non-randomized clinical trials; retrospective studies

Table 3 - Clinical research question identified with the PICOM methodw

Figure 1 – Selection flowchart



RESULTS

Different studies have reported homogeneous results, especially in patients undergoing abdominal and colorectal surgery. In fact, these studies reported a reduction in the perception of pain, compared to patients in the control group, who received opiate drugs and reported several complications. The following data extraction table shows studies results (see Table 4):

DISCUSSION

The studies identified show results that are consistent with the aim of the research, which is to demonstrate that the use of the Enhanced Recovery After Surgery (ERAS*) protocol is more effective than the traditional approach in pain management for patients undergoing abdominal surgery. Sarin et al. (2016) proved that the use of the ERAS* protocol reduced intraoperative opioid consumption and

Title and Author	Year	Journal	Type of study	Results and Discussions
"Predicting delayed discharge in a multimodal Enhanced Recovery Pathway" Keller, Tantchou, Flores-Gonzalez & Geisler	2017	American Journal of Surgery	The study was conducted with the aim of identifying the reasons for the failure of the ERAS [®] protocol and the factors that can lead to longer recovery times, despite the application of the protocol to colorectal surgery.	274 cases were included, 229 were successful and 45 were bankrupt. Bankruptcy is defined as the failure to achieve outcomes due to resignation within a period of 5 days. The reasons for the failure of the protocol were: high rates of preoperative anxiety (OR 2.28), pain (OR 10.03), and previous abdominal surgery.
"Effectiveness of continuous wound infusion of local anesthetics after abdominal surgeries" Dhanapal et al.	2017	Journal of Surgical Research	The study involves two groups of 47 patients who are candidates for abdominal surgery. The experimental group was treated with bupivacaine .25%, the control group with saline .9%. Both treatments were performed with preperitoneal catheterization, at a speed of 6ml/h for 48 hours. All patients received an auxiliary morphine treatment via PCA.	Total morphine consumption was much lower in the experimental group (18.8 ± 2.2 mg) than in the control group (30.8 ± 2.5 mg). The intensity of pain, measured with VAS scale, was lower in the bupivacaine group than in the placebo group. Intestinal functions were resumed early in the experimental group (69 ± 2 hours), compared to the control group (76 ± 3 hours).
"Liposomal bupivacaine use in transversus abdominis plane blocks reduces pain and postoperative intravenous opioid requirement after colorectal surgery" Stokes et al.	2017	Diseases of the Colon and Rectum	Retrospective study in order to evaluate the use of bupivacaine in the blocks of the transverse plane of the abdomen, correlating it to postoperative pain and opioid consumption, in colorectal surgery. The study group consisted of 303 patients, the control group of 104 patients.	Patients prescribed bupivacaine as a pharmacological agent to block the transverse plane of the abdomen had a significant reduction in pain in the first 36 hours after surgery (p <.001). Opioid use was lower in the study group (64.5 mg) than in the control group (99 mg).

Table 4 – Outcomes of ERAS® protocol

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Title and Author	Year	Journal	Type of study	Results and Discussions
"Successful implementation of an Enhanced Recovery After Surgery program shortens length of stay and improves postoperative pain, and bowel and bladder function after colorectal surgery" Sarin et al.	2016	BMC Anesthesiology	The study involved 279 patients who underwent abdominal colorectal surgery using the ERAS [®] protocol, compared to 245 patients who underwent the same type of surgery prior to the implementation of the ERAS [®] program.	The study showed that the introduction of the protocol reduced intraoperative opioid consumption (99 vs 68 mg), opioid demand on the first two postoperative days (75 vs 142 mg), and pain intensity (VAS 2.1 vs 3.2; p <.001). Implementation of the protocol also reduced postoperative recovery times (4.1 vs 6 days), and readmission rates (9.4% vs 21%).
"Enhanced recovery after giant ventral hernia repair" Jensen, Brondum, Harling, Kehlet & Jorgensen	2016	Hernia: The Journal of Hernias and Abdominal Wall Surgery	32 patients undergoing ventral hernia repair according to the ERAS [®] model.	The analysis of the results, focuses on the reduction of recovery times compared to the traditional surgical approach (median of 3 vs 5 days); on the reduction of postoperative pain during the transition from supine to orthostatic position and after a walk of 6 meters.
"The effect of transversus abdominis plane blocks on postoperative pain in laparoscopic colorectal surgery: A prospective, randomized, double- blind trial" Keller et al.	2014	Disease of the Colon and Rectum	Randomized double-blind controlled trial involving 79 patients who underwent laparoscopic colorectal resection surgery in the election. 41 patients were treated with the TAP-Block technique, the remaining 38 patients were part of the control group.	TAP-Block treatment reduces postoperative pain more effectively than the use of opioids (p <.01). Recovery in the experimental group was shorter (median, 2 days), compared to the control group (median, 3 days). The readmission rate was very similar in both cases.
"Transversus abdominis plane blocks and enhanced recovery pathways: Making the 23-h hospital stay a realistic goal after laparoscopic colorectal surgery" Favuzza, Brady & Delaney	2013	Surgical Endoscopy	Study of 70 patients, 35 of whom were treated with TAP-Block, the remainder with a traditional approach.	The mean time for postoperative recovery was 2 days for patients belonging to the experimental group, and 3 days for patients in the control group. The use of opioids in the postoperative group was lower in the experimental group (31.8 mg) than in the non-treated TAP- Block group (85.4 mg). On the first postoperative day, 13 patients treated with TAP-Block and 1 patient in the control group were discharged.

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Title and Author	Year	Journal	Type of study	Results and Discussions
"Intravenous flurbiprofenaxetil accelerates restoration of bowel function after colorectal surgery"	2008	Canadian Journal of Anaesthesia	Prospective, randomized, double-blind, placebo-controlled trial. Randomization was performed on 40 patients,	The experimental group received, 30 minutes before and 6 hours after the surgical incision, an intravenous administration of flurbiprofen, equal to 1 mg/Kg.
Xu, Tan, Chen, Lou & Chen			candidates for colorectal surgery according to the ERAS [®] protocol, divided into two cohorts.	An identical volume of placebo was administered to the control group. The experimental group showed early bowel remission $(87\pm23 \text{ hours})$, compared to the control group (105 ± 19 hours). In the first 24 hours, the experimental group also had better pain control than the placebo group (p <.001).

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decreased postoperative recovery times (4.1 *vs* 6 days) as well as readmission rates (9.4% as against 21%). Jensen et al. (2016) studied 32 patients who underwent hernia surgery and treated with the ERAS[®] protocol.

The analysis of the results highlights the reduction of recovery times compared with traditional surgical approach (3 *vs* 5 days median) and the reduction of postoperative pain.

Xu et al. (2008), in a prospective randomized doubleblind trial, demonstrated that the group of patients assigned to the experimental protocol had a faster intestinal recovery (87 ± 23 hours) compared with the control group (105 ± 19 hours). In addition, in the experimental group, the pain control during the first 24 hours after the operation was better than that of the group treated with a placebo (p<.001). This review confirms benefits of the application of the ERAS^{*} protocol for pain management if compared with a traditional pain treatment. Multimodal analgesia techniques, as used in the ERAS^{*} protocol, allow a better control of postoperative pain in patients undergoing abdominal surgery, both in the first hours after surgery and in the following hours.

The study conducted by Dhanapal et al. (2017) involved two groups of candidates for abdominal surgery. The experimental group was treated with .25% bupivacaine and the control group with a .9% physiological solution. The morphine consumption was lower in the experimental group (18.8±2.2 mg) than in the control group (30.8±2.5 mg). The pain intensity, measured by *Visual Analogic Scale* (VAS), was lower in the group treated with bupivacaine compared to the placebo group.

Stokes et al. (2017) compared the use of bupivacaine and opioid consumption to manage postoperative pain in colorectal surgery. Patients treated with bupivacaine had a significant reduction of pain in the first 36 hours after the operation (p<.001). Moreover, the use of opioids was lower in the treatment group compared to the control group.

As far as opioid consumption is concerned, the results derived from these studies show a marked reduction in the need for morphine in the postoperative period for patients treated with the ERAS[®] protocol. The lower need for opioids in postoperative pain control determines a reduction of the time interval necessary for a full recovery of the intestinal functions, in terms of intestinal activity normalization, oral feeding, and channeling of stool and gas delivery.

The analysis of the results emphasizes the reduction of recovery times compared with traditional surgical approach: patients treated with TAP-Block showed a significant reduction in pain in the first 36 hours after surgery, compared to patients undergoing opioid therapy.

Keller et al. (2014), in a randomized double-blind controlled trial, demonstrated that the TAP-Block treatment

reduces postoperative pain more effectively than opioids treatment (p<.001). Recovery times, in the experimental group, were shorter than in the control group (2 *vs* 3 days median). Favuzza et al. (2013) verified that the mean time for postoperative recovery was 2 days for patients in the experimental group treated with TAP-Block and 3 days for patients in the control group.

Opioid consumption was also lower in the experimental group compared to the control group (31.8 mg *vs* 85.4 mg).

Only one article included in the review is not consistent with the research aim. Keller et al. (2017) have developed this study with the purpose of identifying possible reasons for failure in the ERAS^{*} protocol and the factors which would determine an increase in recovery times. Missing to achieve the outcome of discharge in the first 5 days was considered as a failure. The study included 274 cases and 45 failures were observed. High levels of preoperative anxiety, pain, previous abdominal surgery history were the reasons leading to the failure of the protocol.

CONCLUSIONS

The ERAS^{*} protocol for pain management in abdominal surgery has been shown to be effective in dealing with postoperative pain control, reduction of opioid consumption and early recovery of mobility. In particular, reduction of opioid consumption prevents several conditions such as paralytic ileus and nausea, allowing early resumption of oral feeding and return of normal gastrointestinal activity. Effective pain management does not depend only on the analgesic technique, but also on individual factors. For this reason, it is necessary to consider elements such as knowledge of pain, the meaning that a person gives to it, environmental and social factors, level of stress, the knowledge about surgical procedure and the plan of the postoperative care, family and caregivers responses. Preventive education and psychology preparation for the intervention allow a conscious management of anxiety, a factor that affects the perception of pain, encouraging greater control of postoperative pain. According to ERAS* protocol, postoperative assistance to patients undergoing abdominal surgery is centered on the relationship of help and consists not only in technical but also in relational and educational interventions in order to support and to develop the person and the entire family empowerment. Further implementations in the treatment of pain under the ERAS® protocol for abdominal surgery are expected in the future. Many aspects still required further study to explore the effectiveness of the ERAS® protocol in other surgical realities. It could be very useful to focus further research on aspects such as: a) choice of distinct educational programs for the different stages starting from diagnosis, decision making to the intervention; b) identification of differences in the outcome associated with specific traits of patients' personality; c) identification of the emotional support provided by family, caregiver or psychologist to help patients to face the acute stress associated with surgery; d) elaboration of the long-term outcomes of ERAS® protocols, as assessed through repeated follow-up; e) assessment of the reliability and sensitivity of the measures of pain control and emotion monitoring in facing the distress associated with surgery; f) identification of the clinical, demographic and psychological characteristics of the subgroup of patients who require longer hospital stays than expected based on ERAS® protocol. Finally, these data would be stronger if replicated in multicenter, prospective studies.

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