Non-Inferior Efficiency of Opiod-Free Analgesia Support Among Colorectal Cancer Patients During and After Surgical Treatment: Evidences of Open-Label Trial

Tenkach O.[1], Rusyn A.[1], Palahonych E.[1], Ivachevskyi M.[1], Balazh O.[2], Goncharuk-Komyn M.[2]*

1. Medical Faculty, Uzhhorod National University, Uzhhorod, Ukraine.
2. Medical Faculty №2, Uzhhorod National University, Uzhhorod, Ukraine.

Abstract

Objective of the research was to evaluate an impact of non-opioid anesthetic support during and after surgical treatment of colorectal cancer patients on postoperative rehabilitation results. Considering used inclusion and exclusion criteria primary study sample was formed of 50 patients aged 42-83 years (mean age value – 51.2±5.2 years). Based on planned analgesia support during and after operative intervention primary study sample was divided into study and control groups, consisting of 25 subjects each. Study group received opioid-free analgesia support, while control group was supported with opioid-associated protocol of analgesia. Statistically significant difference considering NRS pain scores between study and control group was noted at the 1st (p < 0.05) and 2nd day (p < 0.05) after surgery, while at the day of surgery and at 3rd and 5th day of monitoring such difference was not statistically argumented (p > 0.05). Restitution of bowel peristalsis among study group patients was noted after mean of 1.5±0.4 days, while within control group after mean of 2.9±0.5 days, which was statistically faster considering distribution pattern specifics among all study cohort (p < 0.05). Post-operative hospital stay among study and control group demonstrated analogical trend: 6.4±0.9 days vs. 9.9±0.2 days (p < 0.05). Considering limitations associated with open-label design of provided study it could be resumed that non-opioid postoperative anesthetic approach provides non-inferior effect on rehabilitation efficiency of colorectal cancer patients in terms of post-operative NRS scores, blood pressure parameters, frequency of nausea and vomiting occurrence, peristalsis recovery and duration of hospital stay. Based on the prospective benefits for multimodal non-opioid anesthetic support within the context of influencing different elements of pain pathogenesis, such approach and its modalities should be considered for the future risk/cost/benefit verification during complex assay of colorectal cancer treatment outcomes.

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Introduction

Pathology of colorectal cancer have been described as 4th the most frequently diagnosed neoplasia in the world, while due to the 2018 GLOBOCAN data colon cancer characterized with much greater prevalence, compare to incidence level of rectum cancer.[1,2,3] Overall near 11% of all diagnosed world cancer cases represented by colorectal form of pathology.[4] In 2020 Cancer.org reported about 147950 new cases of colorectal cancer in USA with correspondence of 104610 among them to colon topography and 43340 to rectum topography.[5] Due to Siegel et al. despite the high registered incidence and mortality rates of colorectal cancer in USA, more than 50% of such clinical cases were associated with modifiable risk factors, so appropriate screening and preventive strategies could positively promote decreasing trend of above-mentioned parameters in the future.[5] Bulletin of National Cancer Registry of Ukraine demonstrated that number of new cases for colon cancer reached 9195, while for rectal cancer 7480 in 2018.[6] Near 21.2-38.2% of newly diagnosed patients received just surgical treatment, while 23.5-33.2% get combined or complex treatment interventions.[6]

Specific trends of colorectal cancer prevalence and mortality rates upgrowth have

Corresponding author:

Goncharuk-Komyn M.,
Medical Faculty №2, Uzhhorod National University, Uzhhorod, Ukraine.
E-mail: myroslav.goncharuk-khomyn@uzhnu.edu.ua

been noted in low- and middle-income countries, while those with high income contrariwise demonstrated decrease pattern of such epidemiological parameters.[2,3,7] Due to the provided systematic analysis for the Global Burden of Disease, it was found that such objectives as preventive strategies implemented though modifiable risk factors, early diagnostics and identification with adequate treatment provision continue to be counted as dominant during further research.[7]

The patient-oriented success of corresponding colorectal cancer treatment is highly correlated with rehabilitation perspectives, considering disease-free survival time, post-operative quality of life, assigned disability level, emotional distress and functional limitations, intensity and prolongation of residual post-surgical pain.[8,9] Changyai et al. reported that colorectal cancer patients who underwent surgical treatment characterized with next four changes arising: suffering, lowered activity level, ambivalent feelings and need for caring.[10] Integrative review supported by number of previously analyzed studies demonstrated that post-operative pain-management playing an important role in recovery prognosis of colorectal patients during short- and long-term monitoring, while personal patient's perception of pain should also be considered by medical support team.[10]

Analysis of different acute pain managements approaches revealed that among number of patients operated due to the colorectal cancer near 35% of respondents noted presence of constant or nearly constant pain.[11] Investigation provided among 2401 patients who underwent colorectal surgery because of cancer pathology demonstrated that among 70.3% of subjects with mild level of pain such has dropped to low, while among 20.0% of subjects with moderate/severe pain such has dropped to mild, but 9.7% of patients demonstrated increased trajectory of moderated pain translation into severe.[12] Lee et al. also pointed that post-operative pain and fatigue feelings among patients who underwent colorectal surgery could represent reasons of patient's refusal for discharge from hospital despite corresponding recommendations.[13]

Moreover, abnormal pain changes trajectories may be related with inferior prognosis of patient's general outcome after colorectal cancer surgery.[12] Major pain associated with quality of life decrease, reduction of cancer-free survival level and frequency of complications within several systems and organs. On the other hand, opiod-associated approaches of post-operative relief also demonstrated some negative effect on future patient's prognosis.[14,15] In cases of postoperative pain chronification or exacerbation, the need for opioids prescription may increase to the level significantly higher than recommended, which is associated with a high risk of complications in the form of suppression within gastrointestinal, circulatory and respiratory systems.[14] In addition, excessive levels of opioids are associated with the potential for further tumor progression and metastases spread.[14,15]

Therefore, adapted evidence-based clinical guidelines for the diagnosis and treatment of colorectal cancer, published by the State Expert Center of the Ministry of Health of Ukraine (2016), contain information on the need for development of comprehensive multidisciplinary approach aimed at pain relief not only with opioids, but also with other drugs, like ketamine and gabapentin.[16] But advantages of approaches that reduce the dose of needed opioids and provide adequate anesthesia in the peri- and postoperative periods with corresponding pain arrest effect, should be justified with further evidences, obtained within various designs of clinical trials.

Objective. To evaluate an impact of non-opioid anesthetic support during and after surgical treatment of colorectal cancer patients on postoperative rehabilitation results.

Materials and methods

Study was conducted within municipal non-commercial facility "Transcarpathian anti-tumor center" of Transcarpathian Regional Council during 2018-2020. Present study design and protocol of its realization was approved by Ethical Committee of Medical Faculty at Uzhhorod National University and assigned with corresponding registration number of EC29344321.

Patients sample was formed from the number of colorectal cancer patients with the need of corresponding surgical intervention due to the following inclusion criteria: 1) histologically approved diagnosis of colorectal cancer; 2) no signs of regional lymphatic nodes involvement into cancer process – N0; 3) no signs of

metastatic cancer spread – M0; 3) cancer lesion grown through the muscularis mucosa into the submucosa layer, or further grown into muscularis propria level – T1 or T2; 4) correspondence of patient current physical status to ASA II or ASA III; 5) need in partial colectomy operation due to the cancer lesion; 6) patient's personal agreement to take part in the study approved by signed informed consent form. Exclusion criteria included the next ones: 1) diagnosed severe heart failure (ejection fraction < 30%); 2) myocardial infarction diagnosed during previous month; 3) disorders of cardiac rhythm or conductivity; 4) signs of regional nodes involvement with cancer lesion – N1, N2, N3; 5) signs of distant metastasis – M1; 6) patients affiliation to ASA > III; 7) need for emergency surgery; 8) pregnancy; 9) inflammatory bowel disease; 10) patient's personal disagreement to take part in the study or refusal to sign informed consent form. Considering used inclusion and exclusion criteria primary study sample was formed of 50 patients aged 42-83 years (mean age value – 51.2±5.2 years). Based on planned analgesia support during and after operative intervention primary study sample was divided into study and control groups, consisting of 25 subjects each. Baseline clinical parameters, which included, age, gender, weight, height and ASA class were registered before any iatrogenic interventions.[17]

Post-operative analgesia support was provided based on specific therapeutic and surgical demands and considerations due to the clinical conditions of each colorectal cancer patient and outcome of provided operation. Proposed analgesia support was preliminary discussed with patient before surgical intervention and personally approved by patient's sign of informed consent form. Such approach excluded possibilities for randomized study design implementation, since aspect of random allocation was diminished. On the other hand, use of strict inclusion and exclusion criteria with equilibrated baseline clinical variables, arguments the possibilities for further non-randomized open-label study realization with outcomes comparison between control and study groups.

This way study group received opioid-free analgesia support, consisted of next algorithm:
1) pre-emptive analgesia (before surgical intervention): pregabalin 150 mg per os 12 hours before operation; acetaminophen 1000 mg intravenously (IV) before cutting the skin layer; MgSO4 25% 2500 mg intravenously before cutting the skin layer; dexamethasone 8 mg intravenously before cutting the skin layer; dexketoprofen 50 mg intravenously before cutting the skin layer;
2) epidural anesthesia at the level of Th XI-XII by standard method. Epidural infusion consisted of 4 ml 0,25% longocain solution used as a control test-dose, and of 0.125% longocain solution in combination with phentanil 2 mkg/ml on infusomat accounted for 5.5-9.5 ml/hour. Induction component consisted of 1% dyprophol solution IV with 2,0 – 2,5 mg on 1 kg of body mass, and atracurium 0,5-0,6 mg/kg 90 seconds after tracheal intubation. Anesthesia support was provided by 1% dyprophol solution on infusomat with 4-10 mkg/kg/hour. Miorelaxation effect was provided by atracurium use in dose of 0.1 – 0.2 mg/kg.
3) preventive analgesia (after completion of operation): nefopam 20 mg/ml with 2.0 ml intramusculary every 8 hours during first day after operation; acetaminophen 1000 mg IV every 8 hours during first 3 days after operation; dexketoprofen 50 mg IV every 8 hours during first 3 days after operation.

Control group was supported with opioid-associated protocol of analgesia:
1) polycomponent general anesthesia: induction component consisted of 1% dyprophol solution IV with 2.0 – 2.5 mg on 1 kg of body mass, and atracurium 0.5-0.6 mg/kg 90 seconds after tracheal intubation. Anesthesia support was provided by 1% dyprophol solution on infusomat with 4-10 mkg/kg/hour. Miorelaxation effect was provided by atracurium use in dose of 0.1 – 0.2 mg/kg.

In both study and control groups patients were activated during the 1st day after operation.

Post-operative nausea and vomiting facts were checked each day during control monitoring for the first 5 days after surgery. Categorization of nausea and vomiting was provided by the 4 patterns previously described in Barclay et al. study: 1) early minimal amounts; 2) early significant amounts with signs of gut disfunction; 3) late minimal amounts; 4) late significant amounts.[18]

Blood pressure parameters and heartrate were registered during first 2 and 8 hours after surgery, and later 3 times per day during first five days after surgery.

Subjective pain grading was held during control clinical check-ups of patients at 8 hours after surgery, and then each day during 5-days monitoring period by numeric rating scale (NRS) with further interpretation: 0 – no pain, 1-3 – mild pain, 4-6 – moderate pain, 7-10 – severe pain.[17] Variations of NRS grades within range of 3 points were considered to represent standard deviation.[17]

General quantitative parameters of the study and control groups were obtained with the use of descriptive statistics considering mean values of age, blood pressure, operation's duration, weight and height. Kolmogorov-Smirnov test was used to verify the normality of distribution, confirmation of which argumented the use of Student's t-criterion for independent samples comparison. Pearson's r was used for bivariate linear correlation estimation with being considered statistically signification only with p-value < 0.05.[19] Linear regression modeling was applied for identification of anesthetic support- and patient-associated parameters influence on research endpoints (outcome blood pressure parameters, intensity of postoperative pain, vomiting and nausea incidence, duration of hospital stay).[20,21] Data accumulation and its categorization was held within Microsoft Excel 2019 software (Microsoft Office, 2019). Table editor was used for data acquisition with further analytical processing by the use of such add-ins, as XLSTAT (Addinsoft) and Analyse-it (Analyse-it Software).

Results

Study cohort
Study group consisted of 14 males and 11 females (mean age value – 49.6±3.7 years), while control group included 16 males and 9 females (mean age value – 56.3±4.1 years). Within 25 patients included in the study group, mean weight was 76.5±17.4 kg, and mean height – 170±9.2 cm. Control group was characterized with mean weight of 78.3±18.1 kg and mean height of 155±39.3 cm. Mean operation time in the study group was 161±37 minutes, while in control group - 155±39 minutes. No statistical difference was noted between study or control

groups' income variables, such as age (p > 0.05), weight (p > 0.05), height (p > 0.05), proportion of males to females (p > 0.05), and operation duration (p > 0.05). Such results characterized balanced condition between study and control groups, which in the combination with used inclusion and exclusion criteria argumented possibility for further outcome variables comparison within non-randomized open-label design of the study.
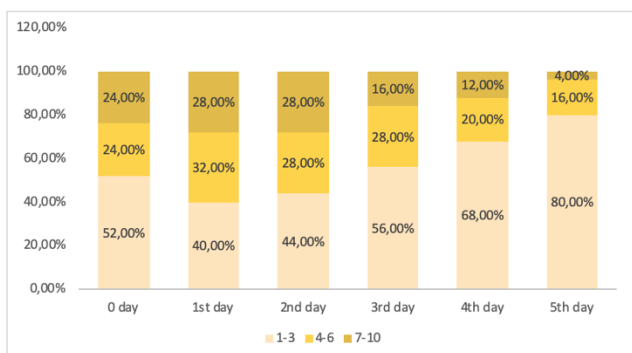
Pain intensity due by NRS scores
Study group revealed the next pattern of pain intensity changes graded by NRS scores: on day 0 – 4.64±2.25; on 1st day after surgery – 5.32±2.79; on 2nd day after surgery – 4.12±2.19; on 3rd day after surgery – 4.02±2.05; on 4th day after surgery – 3.41±1.79; on 5th day after surgery – 2.54±1.52. Control group on the other hand was characterized with next distribution of NRS scores over 5 days of monitoring: on day 0 – 5.02±2.37; on 1st day after surgery – 6.79±2.83; on 2nd day after surgery – 5.53±2.30; on 3rd day after surgery – 4.62±2.14; on 4th day after surgery – 4.08±2.05; on 5th day after surgery – 3.39±1.93. Statistically significant difference considering NRS scores between study and control group was noted at 1st (p < 0.05) and 2nd day (p < 0.05) after surgery, while at the day of surgery and at 3rd and 5th days of monitoring such difference was not statistically argumented (p > 0.05) (Figure 1).
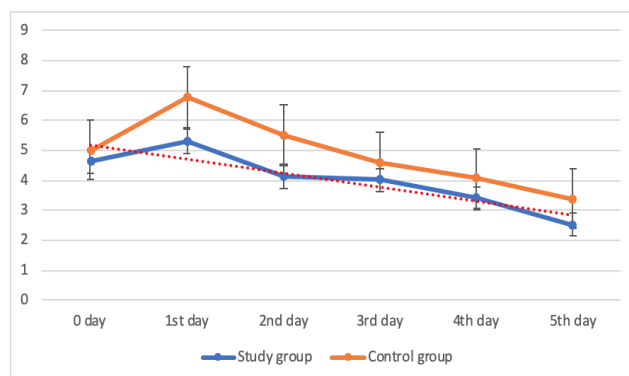

Figure 1. Mean NRS-scores registered among patients of study and control group during 5 days of monitoring after surgery.

Distribution of pain scores graded by NRS approach considering originally proposed intervals demonstrated on Figure 2 for study group and on Figure 3 for control group respectively.

Figure 2. Distribution of NRS-scores among patients of study group considering intervals of pain intensity.
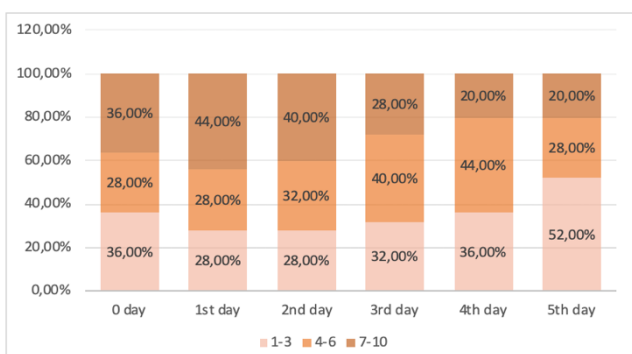
Figure 3. Distribution of NRS-scores among patients of control group considering intervals of pain intensity.

On the day 0, 1st day and 2nd day after surgery statistical difference between groups was noted considering prevalence of pain intensity among patients within intervals of 1-3 and 7-10 points ($p < 0.05$), while prevalence distribution within study and control groups considering pain intensity in interval of 4-6 points was analogical during above mentioned periods of monitoring ($p > 0.05$). Difference of pain NRS intervals distribution between study and control groups was statistically significant for 3rd, 4th and 5th day after surgery ($p < 0.05$). Nevertheless, both groups demonstrated tendencies of prevalence increase considering cases with pain intensity of 1-3 NRS points, and prevalence decrease considering cases with pain intensity of 7-10 NRS points for the 5 days of monitoring. Such pattern indirectly indicates about general decrease of pain intensity among patients operated because of colorectal cancer pathology during on-going monitoring, even though such decrease pattern was not gradual. Non-gradual profile of pain scores descendance potentially could be related with specific mechanism of pain resolution and subjective interpretation of pain provided by patients personally due to NRS grading methodology.

Post-operative nausea and vomiting

Considering used categorization principle of post-operative nausea and vomiting facts described in publication of Barclay et al.,[18] it was noted that statistical difference was registered only in "Late significant amounts" category (1 patient in study group vs. 2 patients in control group), while in other categories distribution pattern was analogical within study and control group ($p > 0.05$) (Table 1).

	Early minimal amounts	Early significant amount with signs of gut disfunction	Late minimal amounts	Late significant amounts
Study group	12.0%	4.0%	16.0%	4.0%
Control group	16 .0%	4.0%	16.0%	8.0%

Table 1. Distribution of registered post-operative nausea and vomiting facts among patients of study and control groups.

Blood pressure and heart-rates parameters

Statistically argumented difference between study and control group considering blood pressure and heart-rates parameters was noted during 0 day of monitoring (day of surgery) ($p < 0.05$), 2nd ($p < 0.05$) and 3rd ($p < 0.05$) days after surgery. Distribution of blood pressure values and heart rate levels registered during 5 days monitoring presented in Table 2.

	0 day		1st day		2nd day		3rd day		4th day		5th day	
	Study group	Control group	Study group	Control group	Study group	Control group	Study group	Control group	Study group	Control group	Study group	Control group
Blood pressure (systolic/diastolic)	119±9/84±8	128±12/8 9±11	124±8/81±9	130±10/8 5±12	122±9/80 ±10	130±11/8 7±10	120±10/8 1±9	130±11/9 0±10	121±10/8 1±9	127±10/8 6±8	125±10/8 0±10	127±9/84 ±10
Heart rate	76±6	82±6	77±6	81±5	75±5	81±6	75±4	80±5	74±5	79±3	74±5	78±4
Statistical difference considering blood pressure	p < 0.05		p > 0.05		p < 0.05		p < 0.05		p > 0.05		p > 0.05	
Statistical difference considering blood pressure	p < 0.05		p > 0.05		p < 0.05		p < 0.05		p > 0.05		p > 0.05	

Table 2. Distribution of registered blood pressure and heart rate parameters among patients of study and control groups.

Restitution of bowel peristalsis

Restitution of bowel peristalsis among study group patients was noted after mean 1.5±0.4 days, while within control group after mean 2.9±0.5 days, which was statistically faster considering distribution pattern specifics among all study cohort (p < 0.05). Post-operative hospital stay among study and control group demonstrated analogical trend: 6.4±0.9 days vs. 9.9±0.2 days (p < 0.05).

No statistically approved influence of such parameters as age or gender were noted on outcome of NRS pain scores during regression analysis (p > 0.05). Neither patients with different weight or height were characterized with statistically significant difference considering subjectively graded pain intensity (p > 0.05). Such tendencies could be related with relatively small study and control group quantities and specific age distribution of patients.

Discussion

Steyaert and Lavand'homme noted that despite all the available progress in pain curation, a large portion of patients continue to report severe pain in first 24-28 hours after surgical interventions.[22] While considering that worldwide amount of operative manipulations exceeds 300 million per year, problem of postoperative pain reduction arises as significantly important challenge of relevant medical practice.[22] In our study we also have noted the greatest level of pain intensity at the day of surgery and during 1st and 2nd days after surgery, while further monitoring demonstrated pain intensity decrease both in study and control groups. Analogical trend was noted also in Lindberg et al. study.[17]

Negative effect of postoperative pain also associated with its tendency to chronification: previously it was noted that nearly 11.8% of patients potentially suffer from pain during more than 3 months after surgery.[22] The presence and duration of postoperative pain associated with the risk of different disorders development among several body systems.[23,24,25,26] The development of respiratory disorders is associated with decreased lung volume and progression of atelectasis and pneumonia. The latter occur due to disruption of normal respiratory muscle activity, suppression of diaphragmatic function and inhibition of respiratory dynamics because of pain effect.

Cardiovascular pathological changes occur due to hyperactivation of the sympathetic nervous system, which leads to an increase in heart rate, heart pressure and myocardial oxygen consumption. Pain also provokes excessive stretching of the gastrointestinal tract, vomiting and nausea, and inhibits gastrointestinal motility. Metabolic pain-associated changes occur due to the activation of sympathetic and hypothalamic components, which in turn lead to hyperglycemia, glucosuria, salt and water retention, stimulation of the renin-angiotensin system, lipolysis and hypercatabolism of proteins.[23,24,25] In addition, it was previously established that the generalization of post-operative pain among cancer patients associated with higher mortality rates.[23,24,25,26] That is why problem of effective post-operative pain management programs implementations has been widely discussed in number of studies, aimed at pain control both at the acute post-surgical period and in long-term perspective after patient's discharge from hospital.[22]

Use of epidural anesthesia in Rimaitis et al. study demonstrated improvement of hemodynamic parameters of patients during 3 days of monitoring compare to the pethidine group,[27,28] while in our study we noted statistical difference of hemodynamic parameters during the day of surgery, and at the 2nd and 3rd day after surgery, even though we have compare opiod-free (including epidural anesthesia) and opiod-associated analgesia supports.

Relatively low levels of nausea and vomiting were reported in number of previous studies considering outcomes registered after surgical treatment of colorectal cancer patients, while results obtained in our study fully corresponded with previously reported data.[18,27,28]

Lindberg et al. noted increase of NRS pain scores during 1st day after surgery compare to the 0 day,[17] while in our study we noticed such pattern during 1st and 2nd days of surgery compare to day of surgery. Nevertheless, we also registered non-gradual decreasing trend of pain intensity among study and control group during 5 days of monitoring, while range of such changes was characterized with pronounced interindividual variability.

In population-based study supported with meta-analysis it was suggested that factors of cancer-associated pain and opioid need are

affiliated with low survival level among patients with advanced cancer pathology. But, authors also mentioned that intense pain couping remains a therapeutic priority, so further research of non-opioids algorithms for anesthetic support continue to be relevant.[14]

Even though some studies demonstrated connection between opioid use and further cancer recurrence, systematic review provided by Diaz-Cambronero et al. suggested that available evidences do not support rejection of opioid use among colorectal cancer patients.[29] Nevertheless, results of above-mentioned systematic review supported two other important points: 1) perioperative time period is of high importance for implementation of targeted therapeutic impact that can reduce risk of further cancer progression; 2) anesthetic support itself demonstrates influence on immune function and cellular behavior considering their "proliferation, invasion and colony formation".[29] Because pain itself is a potential predictor of post-operative outcome, quality of life, survival level and recurrence risk, anesthetic support should be based on individual requirements and personalized needs.

In previous studies it was also mentioned that not only opioid use, but other factors also demonstrated reasonable influence on post-operative pain intensity and survival rate.[30,31,32] Latter includes pre-operative pain amplitude, stage of cancer lesion, patient's age and operation's duration. Even though considering non-randomized open-label design of the study, which was formulated due to the selection of surgical modality chosen by patient himself and proposed by doctor from those available for use (differed only by anesthetic support), we can assume that all of about mentioned factors were balanced between study and control group of patients to the level where it should not provide any statistically significant impact on the research's outcome. Nevertheless, considering non-randomized open-label study design we are not able to conclude that such factors in our study did not provide any clinical impact individually for each patient.

Even though we have not registered any statistically significant influence of age, gender, weight or height parameters on the outcome of NRS pain scores, but obtained results are not eligible to interpret them on overall colorectal cancer patient's population. Such factors as

relatively small study cohort and non-randomized open-label design of the study could diminish the role of above-mentioned variables on efficiency of post-operative analgesia support, so registered trend is strictly affiliated to the analyzed patients' sample and should be analyzed with in-depth manner during future research projects.

With the focus on colorectal cancer Szczepaniak et al. concluded that possible side effects of opioid use should be studied considering several influential aspects, such as used study model, route, mode of administration, exposure duration and type of cancer.[32] Moreover, authors agreed that with the consideration of negative consequences of opioid use among colorectal cancer patients there is relevant practical need of further drug or approach development that can potentially overcome such issues.[32] In current study we presented possible approach of non-opioid anesthetic support that helped to increase derivates of rehabilitation efficiency with non-inferior outcomes compare to opioid-use control group. Even though, study group demonstrated statistically better results considering distribution of NRS-score intervals for pain intensity, faster restitution of bowel peristalsis and more pronounced normalization of blood pressure and heart rate parameters, we prefer to interpret such results as non-inferior rather than more effective, considering non-randomized open-label design of the study, short period of monitoring and relatively small sizes of study and control groups, which represent limitations of provided research.

Considering some inconformity of outcomes reported in previous studies considering advantages and drawbacks of opioid and non-opioid peri- and post-operative approaches, it could be resumed that such could be reasoned by interindividual variability of pain intensity and personal affinity to different drug agents.[33,34,35,36] In present study it was demonstrated that opioid-free perioperative support characterized with non-inferior clinical results regarding pain arrest effect, restitution of bowel motor activity, frequency of vomiting and nausea development and blood pressure changes. Alternatively taking into consideration that opioid use itself potentially may be associated with number of complications, proposed approach of opioid-free anesthesia could be interpreted as effective for the

implementation during surgical treatment of colorectal cancer patients, which positively impact their rehabilitation prognosis during provided short-term monitoring.

Limitations of present study associated with its non-randomized open-label design, which was reasoned by previously agreed anesthetic support due to the therapeutic considerations for specific conditions of each clinical situation. Basically, such aspect excluded possibilities for randomized allocation, but it is worth to mention that study and control groups were preliminary balanced using specific inclusion and exclusion criteria. Design of randomized controlled study could potentially improve outcomes for comparative analysis between opioid and opioid-free groups of patients, while non-randomized open-label design revealed that results registered among opioid-free demonstrated non-inferior endpoint pattern in means of pain reduction effect, peristaltic re-establishment, low nausea and vomiting incidence, shorter hospital stay period. However, such results justified just among presented study sample during short-term monitoring, while greater sample quantity and longer screening periods could be associated with differed tendencies. Such aspects should be categorized as relevant for future studies, while using already obtained results as grounbase for more argumentative conclusion formulation.

Conclusions

Considering limitations associated with open-label design of provided study it could be resumed that non-opioid postoperative anesthetic approach provides non-inferior effect on rehabilitation efficiency of colorectal cancer patients in terms of NRS scores, blood pressure parameters, incidence of nausea and vomiting and peristalsis recovery. Mean duration of hospital stay for study group was statistically shorter compare to control group, and substantial trend of improvement among targeted research parameters within study group indicates about a potential positive economic impact of non-opioid anesthetic approach during surgical treatment of colorectal cancer patients with less possible expanses spend on opioid-associated adverse post-operative consequences. Based on the prospective benefits for multimodal non-opioid anesthetic support within the context of influencing different elements of pain

pathogenesis, such approach and its modalities should be considered for the future risk/cost/benefit verification during complex assay of colorectal cancer treatment outcomes.

Declaration of Interest

The author reports no conflict of interest and the article is not funded or supported by any research grant.

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