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Research Article

Effect of Epidural Anesthesia on Cancer Recurrence after Curative Surgery for Gastrointestinal Cancer

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ABSTRACT

Background: Anesthesia techniques significantly impact the long-term and short-term outcomes after cancer surgery such as cancer recurrence, post-discharge hospitalizations, and duration of hospitalization, probably by decreasing the neuroendocrine stress response during surgery, reducing opioid requirement, reducing post-operation nausea vomiting, and pain, and interacting with the immune system. Research in recent years has provided ample evidence that epidural anesthesia produces better post-operation outcomes compared to general anesthesia. The purpose of this study was to evaluate the effects of epidural anesthesia on cancer recurrence after surgery in gastrointestinal cancer patients.

Methods: To perform this study medical records from the archive of gastrointestinal cancer patients who have undergone surgery at Imam Khomeini Hospital Complex (IKHC) from the years 1390 to 1400 were used. The variables required for the study were obtained from the records. The data obtained were analyzed by the SPSS software and the significance value of < 0.05 was considered.

Results: Our study included 8987 patients out of which 1673 patients received epidural anesthesia. Cancer recurrence was reported after 90 days and 180 days and for the type of surgery (using or not using epidural anesthesia) B value for 90 days and 180 days was 0.079 and 0.018 respectively. Thus causality was not established for the type of surgery with recurrence of cancer.

Conclusion: The findings of our study indicate that the rate of gastrointestinal cancer recurrence after surgery is not influenced by having or not having epidural anesthesia.

Introduction

Cancers are caused by a blend of heritable and environmental factors. Due to insufficient information about the pathophysiology of various cancers and ways of their prevention, they are a subject of colossal exploration [1]. Gastrointestinal cancers contribute to a large percentage of cancers and their incidence and prognosis greatly varies among different sites of the digestive tract [2]. Cancer being the third most common cause of death in Iran, causes 30,000 deaths annually while half of the deaths due to cancer are attributed to gastrointestinal cancers only [3]. Resection of localized tumors remains the top element of treatment and implicit cure for a bulk of solid malignancies, in addition, chemotherapy, radiotherapy, and palliative care may be included in cancer treatment strategies [4]. Anesthesia and analgesia help to bring down the post-operative complications probably by reducing pain, post-operative nausea vomiting, and even the post-operative ileus. The objective of sedation and general anesthesia is to ensure patient comfort and well-being and help them to revive and return to their pretreatment condition at the time of discharge. The epidural technique in itself is a pronounced advancement in the field of anesthesia and is gaining swift acceptance due to the perceived reduction in morbidity and overall case satisfaction [5]. Additionally, reduced chances of DVT, lowered blood loss and shorter duration of surgery are some of the

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known merits of epidural anesthesia over general anesthesia [6]. Anesthetic techniques may also help reduce cancer recurrence and increase post-operative survival by reducing the surgery-related inflammatory process and by reducing the anesthetic and opioid consumption [7]. However various potential benefits of epidural anesthesia are yet to be explored and it may give a breakthrough in the medical field in the upcoming years. Therefore we tried to study the effects of epidural anesthesia on cancer recurrence in gastrointestinal cancer patients after surgical resection of the cancer.

Methods

To perform this study medical records from the archive of gastrointestinal cancer patients who underwent surgery at Imam Khomeini Hospital Complex (IKHC) from the years 1390 to 1400 were used. The variables required for the study were obtained from the records. The data obtained were analyzed by the SPSS software using univariate regression analysis and the P value of < 0.05 was considered for a significant relationship between variables.

Results

At the end of our data collection, we had 53226 patients out of which we included 8987 patients in our study who had no missing data. Among these 4250 were females and 4737 were males. The mean age of the patients included in our study was 53.47 years. The mean duration of hospitalization was 8.5 days with a standard deviation of 8.74. The average duration of hospitalization for patients who received epidural anesthesia was 9.13 days with a standard deviation of 7.38 and for those without epidural anesthesia was 8.37 with a standard deviation of 9.08. Out of 8987 patients, 1673 (18.62%) received epidural among which 705(42%) were females and 968 (57%) were males and the mean age of patients who received epidural anesthesia was 55.53 years. For recurrence in terms of requirement of chemotherapy, from a total number of 8987 patients, 765 patients had recurrence (required chemotherapy) after 90 days and 537 patients had recurrence after 180 days, from those 1673 patients who received epidural anesthesia 185 patients had recurrence after 90 days and 134 patients had recurrence after 180 days, from those 7314 patients who did not receive epidural 580 patients had recurrence after 90 days and 403 patients had recurrence after 180 days. According to our univariate linear regression analysis, the B value for age in relation to the duration of hospitalization is 0.037, for gender, it is -0.906, for the type of surgery (having or not having an epidural) it is 1.035, therefore a causality between age, gender, and type of surgery has been established. Therefore, age and the use of epidural anesthesia have a direct relation while female gender has an inverse relation with the length of hospital stay (Table 1). Also, the B value for age relation with cancer recurrence is -0.0034(for the 90-day group) and -0.0018 (for the 180-day group), for gender the B value is 3.05 and -0.0107 respectively, for the type of surgery the B value is -0.079 and 0.018 respectively hence causality has not been determined for any of these variables with recurrence of cancer (Table 2).

Table 1- Logit regression of the length of staying in hospital on dependent variables with ward FE

Variables	(1) Duration of hospitalization
age	0.0365***
	(0.00661)
Gender(female)	-0.906*** (0.201)
Type of Surgery: (Use of epidural anesthesia)	1.035*** (0.250)
Constant	7.268*** (0.448)
Ward FE	yes
Observations	7,588
R-squared	0.027

Standard errors in parentheses *** p<0.01, ** p<0.05, * p<0.1

Table 2- Logit regression of recurrence after 90 days (model 1) and recurrence after 180 days (model 2) on dependent variables with ward FE

Variables	(1) Model 1 rec 90	(2) Model 1 rec 180
age	-0.00335	-0.00181
	(0.00330)	(0.00364)
Gender(female)	3.05e-05	-0.0107
	(0.0916)	(0.101)
Type of surgery (use of epidural anesthesia)	-0.0797	0.0180
	(0.112)	(0.123)

Constant	0.136	0.0733
	(1.421)	(1.422)
Observations	2,212	2,212

Standard errors in parentheses *** p<0.01, ** p<0.05, * p<0.1

Discussion

In this retrospective cohort study, the major goal was to determine the effect of epidural anesthesia on tumor recurrence in patients who underwent gastrointestinal cancer surgery at Imam Khomeini Hospital Complex in the years 1390 to 1400, and the variability based on age and gender was determined, also, the effect of these variables on duration of hospitalization after gastrointestinal cancer surgery was determined in this study. Our regression analysis has shown that gender was not a predictor for the recurrence of cancer in both the 90-day and 180-day analysis (B= 3.05 and -0.0107 respectively) so there is not a significant difference between cancer recurrences in males and females after surgery. Also, in some similar studies gender was not considered to be a predictor for early recurrence of gastric cancer after surgery may be because this study had a small sample size and was retrospective, a significant relationship gender and cancer recurrence could not be found [8].

In our study relationship between age and recurrence of gastrointestinal cancer was studied which has shown that age was not a predictor for the recurrence of cancer in both the 90-day and 180-day analysis groups (B= -0.0034 for the 90-day group and -0.0018 for 180-day group) however WM Kang in his study found a significant relation between age and early recurrence of gastric cancer after surgery [8]. This may be because the age of our target population was 53 years and if more age groups were included in our study a causality of age for cancer recurrence could have been determined.

Our findings appear to be in agreement with the results of the study performed by Kenneth C. Cummings III, where patients with non-metastatic gastric carcinoma were studied and the overall treated recurrence was 25.6% (27.5% epidural and 24.9% nonepidural). In the adjusted logistic regression, there was no difference in recurrence (odds ratio, 1.40; 95% confidence interval [CI], 0.96–2.05). Median survival did not differ by 28.1 months (95% CI, 24.8–32.3) in the epidural versus 27.4 months (95% CI, 24.8–30.0) in the nonepidural groups. The marginal Cox models showed no association between epidural use and mortality (adjusted hazard ratio, 0.93; 95% CI, 0.84–1.03). Hence it was concluded that there was no difference in groups with or without epidural anesthesia [9]. Our regression analysis has shown that the type of surgery (with or without epidural anesthesia) was not a predictor for of recurrence of cancer in both the 90-day and 180-day analysis (B= -0.079 and 0.018 respectively) which means that having or not having an epidural does not influence the cancer recurrence after the gastrointestinal cancer surgery. The similarity between the results may be due to insufficient data and the retrospective nature of the studies, further prospective studies are needed to provide stronger evidence.

In addition to post-surgical recurrence, we tried to determine the relation between age, gender, type of surgery (using or not using epidural anesthesia), and duration of post-operation hospitalization, and all three factors seemed to be predictors for the duration of post-operation hospitalization.

We have found a direct proportionality of age with duration of hospitalization (B= 0.037) which means the more the age the longer the duration of hospitalization. However, In a study performed by JY Lee, A total of 477 patients admitted to the intensive care unit after gastrointestinal cancer surgery between March 2018, and February 2020, were classified into 3 groups according to age: young (<65 years), older (65–79 years), and oldest (≥80 years) groups, their disease severity scores as well as postoperative and clinical outcomes including length of hospital stay were compared, however no significant differences in various postoperative and clinical outcomes, including length of hospital stay were seen [10] and thus in contrast to our study it was concluded that the older population can successfully undergo major operations if adequate perioperative management is provided. This difference in results may be because in our study the patients had more coexisting diseases or presented with advanced stages of cancer which was responsible for the longer hospital duration.

Also, in our study gender seems to be a predictor for the length of hospital stay with the female gender requiring less number of days of hospitalization post operation (B=-0.906), this may be because females are not preferred for many invasive procedures compared to males so this may eventually lead to shorter hospital stays in females.

In our study using epidural anesthesia is associated with an increase in the duration of hospital stay(B=1.035,), Similar results have been shown in a study performed by Halabi WJ, Kang CY where The Healthcare Cost and Utilization Project Nationwide Inpatient Sample (NIS) database was retrospectively analyzed for elective laparoscopic colorectal procedures performed with or without the use of epidural analgesia between January 1, 2002, and December 31, 2010, and it was concluded that the use of epidural analgesia was associated with an increase in length of stay by more than half a day [11]. This finding may be explained by the additional time required to transition patients to other forms of

conventional analgesia as well as removing the bladder catheter, which typically occurs a few hours after the epidural catheter is removed although for our study there is limited information about the what anesthetic drugs were used and how they were used. Thus, with ample data, we may arrive at different results.

Conclusion

In this descriptive review, we presented the effect of epidural anesthesia on cancer recurrence in patients who underwent gastrointestinal cancer surgery. Also, the effect of demographical factors like age and gender on cancer recurrence was determined and none of these factors was found to be associated with cancer recurrence. As for age, it was not a predictor for cancer recurrence maybe because extremes of age groups were not present for the study, which may be due to death or no follow-up, which is one of the limitations of this study, for epidural anesthesia the composition of drugs used for anesthesia or the techniques of their usage are not known to evaluate the effects of epidural anesthesia on cancer recurrence which signifies the need of further studies in this area. Also determining the relation between epidural anesthesia and demographic factors on post-surgery length of hospital stay we concluded that epidural anesthesia and increased age are associated with increased duration of hospital stay maybe due to the more advanced cancer and comorbidities in patients which eventually led to longer hospital stays. However, female gender was associated with a shorter hospital stay. In our future studies, we can include larger sample sizes with diverse age groups and evaluate more effects of epidural anesthesia to validate these findings.

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