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Original Research Article

Open versus laparoscopic colectomy - which is better from immunity-point of view: three-year single-center retrospective study

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ABSTRACT

Background: Objective of the study was **e**valuation of the impact of colorectal surgery on patients' immune milieu through comparison of outcomes of patients had open colectomy (OC) versus laparoscopic colectomy (LC) for colorectal carcinoma (CRC).
Methods: The design of the study was retrospective observational study. The study setting was Mediclinic Airport Road Hospital, Abu Dhabi, UAE. Files of CRC patients who had LC (group-LC) or OC (group-OC) were revised for perioperative data and estimated serum inflammatory cytokines' levels. Statistical analyses of the relation between the postoperative (PO) outcomes and serum cytokines' levels estimated in samples obtained immediately PO.
Results: Patients underwent LC had significantly lower amount of operative bleeding and shorter operative time with lower frequency of patients required ICU and shorter duration of ICU stay. LC provided lower pain scores with shorter duration till 1st ambulation and passage of flatus and shorter duration of hospital stay. LC significantly reduced serum cytokines' levels in immediate PO samples of LC than OC patients. At 1-week PO, serum cytokines' levels were significantly lower than in immediate PO samples with significant difference between LC and OC samples. Moreover, epidural anesthesia (EA) and opioid-free general anesthesia (GA) had lower serum cytokines' levels than opioid-based GA. Statistical analyses defined laparoscopic surgery under EA and non-opioid analgesia as the highly significant predictor for favorable PO surgical outcomes and proper control on surgical immune response.
Conclusions: LC significantly improved PO surgical outcomes and attenuated the surgical immune response with significant difference than OC. EA juxtaposed with opioid-free analgesia significantly provided further control on the surgical immune response.

Keywords: Colorectal carcinoma, Laparoscopy, Open surgery, Inflammatory cytokines

INTRODUCTION

Colorectal cancer (CRC) is rated as the third most common cancer worldwide and the most common gastrointestinal cancer that mostly affect right colon, which accounts for 40-45% of cases of CRC.[1]

Surgery is ideal treatment option for CRC and minimally invasive methods such as laparoscopic colectomy (LC) are the preferred procedures. However, anatomical complexity and variations in vessel branching patterns pose challenges on LC especially for less experienced surgeons.[2]

Surgical interference for cancer deregulates the immune milieu systemically and in cancer adjacent normal tissue across different cancers mostly due to exposure of tissue to mechanical stress leading to rapid gene expression changes.[3]

Recent studies assured the efficacy of laparoscopic surgery for gastrointestinal cancers as regards the surgical outcomes and the surgical stress immune response, where Zhang et al reported faster gastrointestinal recovery, better postoperative (PO) nutritional status, and comparable oncological outcomes after laparoscopic gastrectomy for patients had locally advanced gastric cancer after neo-adjuvant chemotherapy than open gastrectomy.[4] Also, Sheng et al found laparoscopic cholecystectomy with choledochojejunostomy for gall bladder cancer offers better PO course with short hospital stay and reduction of complications and immune stress response.[5] Further, Ling et al documented that laparoscopic radical gastrectomy is more suitable approach for the treatment of gastric cancer and can reduce the inflammatory response and promote the immune function of these patients in comparison to open radical gastrectomy.[6]

Hypothesis

Surgical stress immune response superimposed on the cancer-related immune deregulation may deleteriously affect the PO course of CRC patients subjected to surgical management, thus manipulations to minimize these effects are mandatory. The study hypothesis is that laparoscopic surgery might minimize the surgical stress with subsequent improved immune milieu and surgical outcomes.

Objectives

This study tried to illustrate the impact of colorectal surgery on patients' immune milieu through comparison of outcomes of patients had open colectomy (OC) versus LC for CRC.

METHODS

Design

It was a retrospective observational comparative study.

Setting

The study was conducted at the Mediclinic Airport Road Hospital, Abu Dhabi, UAE

Study protocol

The protocol of the current study entails exploration of file registry for CRC patients who had surgical excision through four-year duration from January 2020 till Dec 2023. Considering the study design as retrospective file exploration ethics committee had waved for approval and sample size calculation. Files were revised for patients' demographic and medical data, cancer-related data according to preoperative investigations, operative data including the applied procedure; laparoscopic or open, duration of surgery, the frequency of shift of laparoscopic to open, the frequency of intraoperative (IO) complications, the type of anesthesia; general or epidural, type of IO analgesia, the need for PO ICU admission with or without mechanical ventilation, and the duration of ICU stay. As regards PO duration, PO analgesia, the frequency of PO nausea and vomiting, duration till 1st mobilization and 1st passage of flatus, duration of PO hospital stay, the frequency and severity of PO complication. The results of preoperative and PO investigations, data concerning immune biomarkers were also collected. The obtained data were analyzed in relation to the changes in the levels of the estimated immune biomarkers.

Exclusion criteria

Files missing data, files of patients underwent colectomy for indications other than CRC, patients with superimposed immune disorders or maintained on immunosuppressive therapy for any indication were excluded.

Inclusion criteria

Files of patients had colectomy for CRC and were free of exclusion criteria.

Grouping

The files fulfilling the inclusion criteria were categorized according to the operative procedure into open (group-OC) and laparoscopic (group-LC) groups.

Study outcomes

The primary outcome is detection of the differences in the estimated levels of serum cytokines between patients of both groups.

The secondary outcomes were: the differences between preoperative and PO estimated cytokines' levels, the relation between PO findings and PO serum cytokines' levels, and determination of the predictors for PO outcomes.

Statistical analysis

Statistical analyses were performed using IBM® statistical package for the social sciences (SPSS) ® Statistics software (Version 22, 2015; Armonk, USA). The significances of the intragroup differences were assessed using one-way analysis of variance (ANOVA) test, and Chi-square test for the differences in percentage of data. Correlation between the estimated PO findings and serum cytokines' levels was performed using Pearson's correlation analysis. Multivariate regression analysis was used to verify the correlated variates as predictors for PO outcomes.

The receiver operating characteristic (ROC) curve analysis was conducted to the differentiating parameters for PO outcomes as judged by area under the curve (AUC) and its significance in relation to the area under the reference line

(AUC=0.5). The optimum cut off point for significance was p<0.05.

RESULTS

The preliminary exploration of the file registry defined 172 files for patients who underwent colectomy during the duration from January 2020 till December 2023. Seventeen files were excluded; 10 files of patients had colectomy for indications other than CRC, 4 patients had previous surgeries and 3 patients were maintained on immunosuppressive therapy (Figure 1). According to the operative procedure, files were categorized into group-OC included 91 files (58.7%) and group-LC included 64 files (41.3%). Demographic data of patients of both groups showed insignificant differences as shown in Table 1.

Table 1: Patients' demographic and clinical data.

Variables	OC (n=91) (%)	LC (n=64) (%)	P value
Age (years)	55.9±8.3	58.3±7.6	0.078
Gender			
Male	61 (67)	45 (70.3)	0.605
Female	30 (33)	19 (29.7)	
Body mass index (kg/m²)	31.4±2	31.3±1.6	0.701
ASA grade			
ASA-I	21 (23.1)	17 (26.5)	0.666
ASA-II	46 (50.5)	34 (53.1)	
ASA-III	24 (26.4)	13 (20.4)	
Other medical problems			
Yes	18 (19.8)	10 (15.6)	0.508
No	73 (80.2)	54 (84.4)	

Data are shown as mean, standard deviation, percentages; p indicates the significance of difference between both groups; ASA: American Society of Anesthesiologists

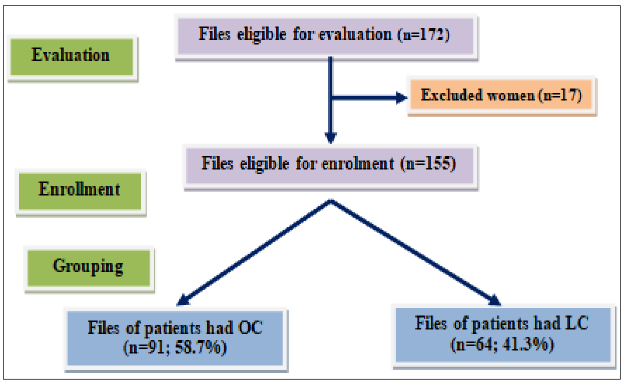

Figure 1: Study flow chart.

Seventy-five patients (48.4%) had right colectomy, 26 patients (16.8%) had left colectomy and fifty-four patients (34.8%) had sigmoidectomy with insignificant (P=0.908) difference between patients of both groups. Sixty-eight tumors (43.9%) were of stage-I, thirty-five tumors (22.6%) were stage-O, thirty-one patients (20%) tumors were of stage-II and twenty tumors (12.9%) were of stage-III, while only one patient had tumor of stage-IV. Patients' distribution according to tumor stage showed insignificant (p=0.749) difference between both groups. Forty patients received epidural anesthesia (EA), while 115 patients received general anesthesia (GA) with significantly (p=0.040) higher frequency of patients received EA among those of group-LC than group-OC. Regarding GA, 51 patients received opioid-free, while 64 patients received opioid-based GA with significantly (p=0.036) higher frequency of patients received opioid-free GA among group-LC than group-OC. Operative time was significantly (p<0.001) longer and IO blood loss was significantly (p<0.001) greater with open than laparoscopic surgery. Four patients of group-LC required shift to open procedure for the presence of adhesions difficult to dissect laparoscopically, so further statistical analysis included 60 patients in group-LC and 95 patients in group-OC (Table 2).

Table 2: Tumor-related and operative data of patients of both groups.

Variables	OC (n=91) (%)	LC (n=64) (%)	P value
Site			
Rt. colon	43 (47.3)	32 (50)	0.906
Lt. colon	15 (16.5)	11 (17.2)	
Sigmoid colon	33 (36.2)	21 (32.8)	
Stage			
0	18 (19.8)	17 (26.6)	0.749
I	42 (46.2)	26 (40.6)	
II	19 (20.8)	12 (18.8)	
III	11 (12.1)	9 (14)	
IV	1 (1.1)	0	
Anesthesia			
General	73 (80.2)	42 (65.6)	0.040
Epidural	18 (19.8)	22 (34.4)	
Type of general anesthesia			
Opioid-based	46 (63)	18 (42.9)	0.036
Opioid free	27 (37)	24 (57.1)	
Operative time (min)	195±34.2	154±38.8	<0.001
Intraoperative blood loss (ml)	529.5±164	186±43.6	<0.001
Shift to open surgery	-	4 (6.25)	-

Data are shown as mean, standard deviation and percentage; p indicates the significance of difference between both groups

All patients were admitted immediately to PACU, but duration of PACU stay was significantly (p=0.012) longer for patients of group-OC than those of group-LC. Unfortunately, 12 patients (7.7%) required ICU admission and three of them were maintained on mechanical ventilation with insignificantly (p=0.233) lower frequency of patients admitted to ICU with insignificantly lower frequency of patients required mechanical ventilation. During PO course maximal pain score was significantly (p<0.001) lower for patients of group-LC than patients of group-OC. Regarding PO analgesia, 63 patients received opioid and 92 patients received non-opioid analgesia with insignificantly (p=0.775) lower consumption of opioid among patients of group-LC. Times to 1st ambulation and 1st passage of flatus were significantly (p<0.001) lower with laparoscopic than open surgery. The frequency of patients complained of PO nausea was significantly (p=0.038) lower, while the frequency of vomiting and need for antiemetic therapy was insignificantly (p=0.295 and 0.164, respectively) lower in group-LC than group-OC. The frequency of patients who developed surgical wound infection was significantly (p=0.033) higher with open than laparoscopic surgery. PO hospital stay was also significantly (p<0.001) longer with open than laparoscopic surgery (Table 3).

Table 3: PO data of patients of both groups.

Variables	OC (n=95) (%)	LC (n=60) (%)	P value
Duration of PACU stay (min)	54±13	48.6±12.9	0.012
ICU data			
Number of ICU admitted patients	9 (9.5)	3 (5)	0.233
Need of mechanical ventilation	2 (2.1)	1 (1.7)	0.700
Duration of ICU stay (d)	48±17	40±13.9	-
PO pain			
Maximal pain score	5±1	2.85±0.85	<0.001
PO analgesia			
Opioid	37 (38.9)	26 (36.7)	0.775
Non-opioid	58 (61.1)	34 (63.3)	
Time to 1st ambulation (h)	15±4.1	8±2.1	<0.001
Time to 1st passage of flatus (d)	4.2±1.7	2.9±0.9	<0.001
PO care			
PO nausea and vomiting			
Nausea	22 (23.2)	6 (10)	0.038
Vomiting	7 (7.4)	2 (3.3)	0.295
Antiemetic	11 (11.6)	3 (5)	0.164
Surgical wound infection	13 (13.7)	2 (3.3)	0.033
PO hospital stay (d)	10.2±1.8	5.6±1.1	<0.001

Data are shown as mean, standard deviation and percentage; p indicates the significance of difference between both groups; PO: postoperative; PACU: post-anesthetic care unit; ICU: intensive care unit

Preoperative cytokines' levels showed insignificant differences between patients of both groups. Immediate PO samples showed significantly (p<0.001) higher cytokines' levels in comparison to preoperative levels in samples of patients of both groups. At 1-week PO, serum cytokines levels decreased significantly in comparison to levels estimated in immediate PO samples for patients of both groups. Immediate PO serum levels of IL-6 and TNF-α estimated in samples of group-LC were significantly (p<0.001 and p=0.011, respectively) lower compared to samples of group-OC, while serum levels of IL-1β were insignificantly (p=0.085) lower. Serum cytokines levels estimated in 1-week samples of patients of group-L were significantly lower in comparison to levels estimated in 1-week samples of patients of group-OC (Table 4 and Figures 2-4).

Table 4: Kinetics of the studied serum cytokines estimated in samples of patients of both groups.

Cytokine, time and group	OC (n=95)	LC (n=60)	P value
Serum IL-6 (ng/ml)			
Preoperative	9.08±1.7	8.8±1.5	0.263
PO			
Level	12.9±2.7	10.7±1.9	<0.001
P1	<0.001	<0.001	
1-w PO			
Level	10.4±2.1	9.04±1.6	0.001
P2	<0.001	<0.001	
Serum TNF-α (ng/ml)			
Preoperative	25.42±9.2	23±9.05	0.116
PO			
Level	33.1±10.9	28.8±9.8	0.011
P1	<0.001	0.0014	
1-w PO			
Level	26.38±8.9	22.5±7.2	0.0053
P2	<0.001	0.0002	
Serum IL-1β (ng/ml)			
Preoperative	34.3±6.4	32.3±6.8	0.066
PO			
Level	40.1±7.3	38.1±7.9	0.085
P1	<0.001	<0.001	
1-w PO			
Level	37.08±6.6	29.8±5.4	<0.001
P2	0.0041	<0.001	

Data are shown as mean and standard deviation; p indicates the significance of difference between both groups; P1 indicates the significance of difference between levels estimated in preoperative and immediate PO samples; P2 indicates the significance of difference between levels estimated in immediate and 1-wk PO samples

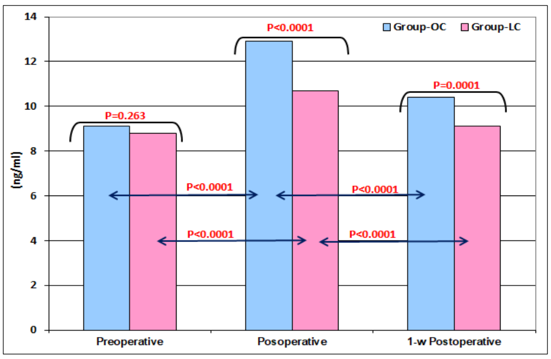

Figure 2: Kinetics of serum IL-6 in samples of patients of both groups.

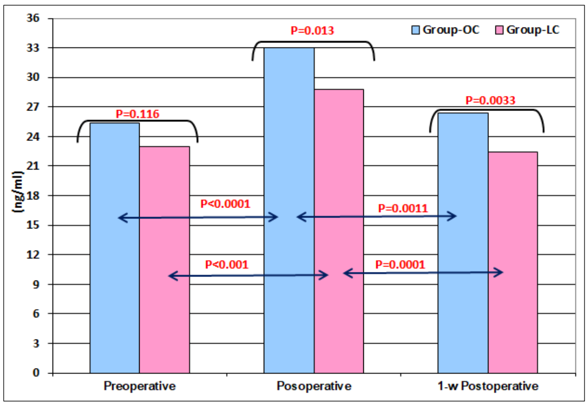

Figure 3: Kinetics of serum TNF-α in samples of patients of both groups.

Evaluation of technical and lab variates as predictors for low PO pain scores using ROC curve analysis defined the use of laparoscopic technique as the highly significant specific predictor especially with the use of IO non-opioid analgesia, while low serum IL-6 in the immediate PO sample is a significant screening variate for the prediction of low PO pain scores (Figure 5a). Regression analysis defined laparoscopic surgery under EA with non-opioid analgesia as the significant predictor for low PO pain scores (Table 5).

The ROC curve analysis defined receiving laparoscopic surgery under EA with or without non-opioid analgesia as the highly significant specific predictors for short time till 1st ambulation, while low PO pain scores and serum IL-6 level in the immediate PO sample were the highly significant sensitive predictors for the oncoming early ambulation. Laparoscopic surgery under opioid-free GA was a weakly significant predictor for short duration till ambulation (Figure 5b).

Regression analysis assured the highly significant predictability of receiving laparoscopy under opioid free EA as the only significant predictor for early PO ambulation and receiving laparoscopy under EA with opioid analgesia is weakly significant predictor (Table 7).

For prediction of short duration till 1st passage of flatus, ROC curve analysis defined the application of laparoscopy under EA and low serum IL-6 in immediate PO samples as the highly significant (p=0.009), while respecting the type of analgesia and low serum levels of TNF-α as weakly predictors for early passage of flatus (Figure 5c). Regression analysis defined laparoscopy under epidural anesthesia as the only highly significant, while low serum IL-6 as significant predictor for early passage of flatus (Table 5).

Laparoscopic surgery under EA (p=0.001) or general opioid-free (p=0.002) anesthesia are the highly significant predictors for short duration of hospital stay, while low PO pain scores and low serum levels of IL-6 (p=0.016) and TNF-α (p=0.046) as significant predictors for early hospital discharge as defined by ROC curve analysis (Fig. 5d). Regression analysis defined laparoscopy under EA as highly significant (p<0.001), and low serum level of TNF-α (p=0.003) was significant predictors for short duration of PO hospital stay, while low serum IL-6 was weakly significant (p=0.021) predictor (Table 5).

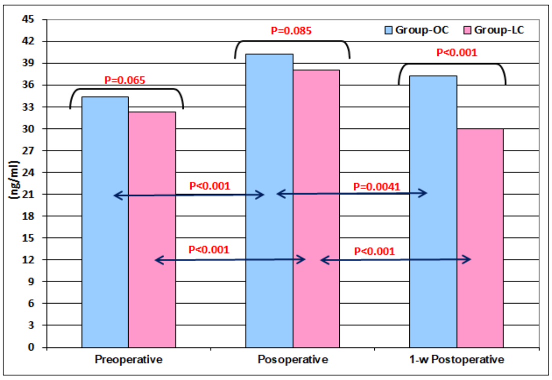

Figure 4: Kinetics of serum IL-1β in samples of patients of both groups.

Table 5: Statistical analyses of the technical and lab variates as predictors for PO outcomes.

Analysis variates	ROC curve				Regression	
	AUC	Standard	P	95% CI	β	P
Low PO pain						
Laparoscopy + EA	0.834	0.034	<0.001	0.767-0.901	0.084	0.355
Laparoscopy + EA + non-opioid analgesia	0.863	0.029	<0.001	0.806-0.919	0.743	<0.001
Laparoscopy + GA + non-opioid analgesia	0.594	0.066	0.145	0.464-0.723	0.051	0.355
Immediate PO serum levels of						
IL-6	0.244	<0.001	0.051	0.145-0.344	0.048	0.383
TNF-α	0.417	0.197	0.061	0.297-0.537	0.043	0.433
IL-1β	0.423	0.229	0.066	0.293-0.552	0.013	0.822
Short duration till 1st ambulation						
Laparoscopy + EA	0.842	0.033	<0.001	0.780-0.931	0.202	0.034
Laparoscopy + EA + non-opioid analgesia	0.856	0.038	<0.001	0.776-0.907	0.545	<0.001
Laparoscopy + GA + non-opioid analgesia	0.670	0.076	0.026	0.520-0.820	0.112	0.061
PO pain score	0.212	0.044	<0.001	0.126-0.229	0.035	0.684

Continued.

Analysis variates	ROC curve				Regression	
	AUC	Standard	P	95% CI	β	P
Immediate PO serum levels of						
IL-6	0.228	0.048	<0.001	0.135-0.321	0.042	0.511
TNF-α	0.361	0.067	0.070	0.229-0.493	0.099	0.093
IL-1β	0.459	0.084	0.593	0.294-0.624	0.067	0.247
Short duration till 1st passage of flatus						
Laparoscopy + EA	0.634	0.050	0.009	0.536-0.732	0.329	<0.001
Laparoscopy + EA + non-opioid analgesia	0.630	0.051	0.011	0.530-0.729	0.024	0.755
Laparoscopy + GA + non-opioid analgesia	0.553	0.052	0.301	0.451-0.655	0.039	0.755
PO pain score	0.433	0.052	0.193	0.332-0.535	0.131	0.238
Immediate PO serum levels of						
IL-6	0.366	0.047	0.009	0.273-0.459	0.189	0.020
TNF-α	0.389	0.050	0.031	0.292-0.487	0.144	0.052
IL-1β	0.471	0.052	0.572	0.369-0.573	0.033	0.657
Short duration of hospital stay						
Laparoscopy + EA	0.825	0.042	0.001	0.734-0.907	0.841	<0.001
Laparoscopy + EA + non-opioid analgesia	0.807	0.053	0.320	0.704-0.910	0.053	0.259
Laparoscopy + GA + non-opioid analgesia	0.599	0.103	0.002	0.397-0.800	0.087	0.259
PO pain score	0.251	0.067	0.012	0.120-0.382	0.009	0.890
Immediate PO serum levels of						
IL-6	0.260	0.072	0.016	0.118-0.401	0.114	0.021
TNF-α	0.301	0.052	0.046	0.199-0.404	0.135	0.003
IL-1β	0.415	0.081	0.391	0.257-0.573	0.056	0.222

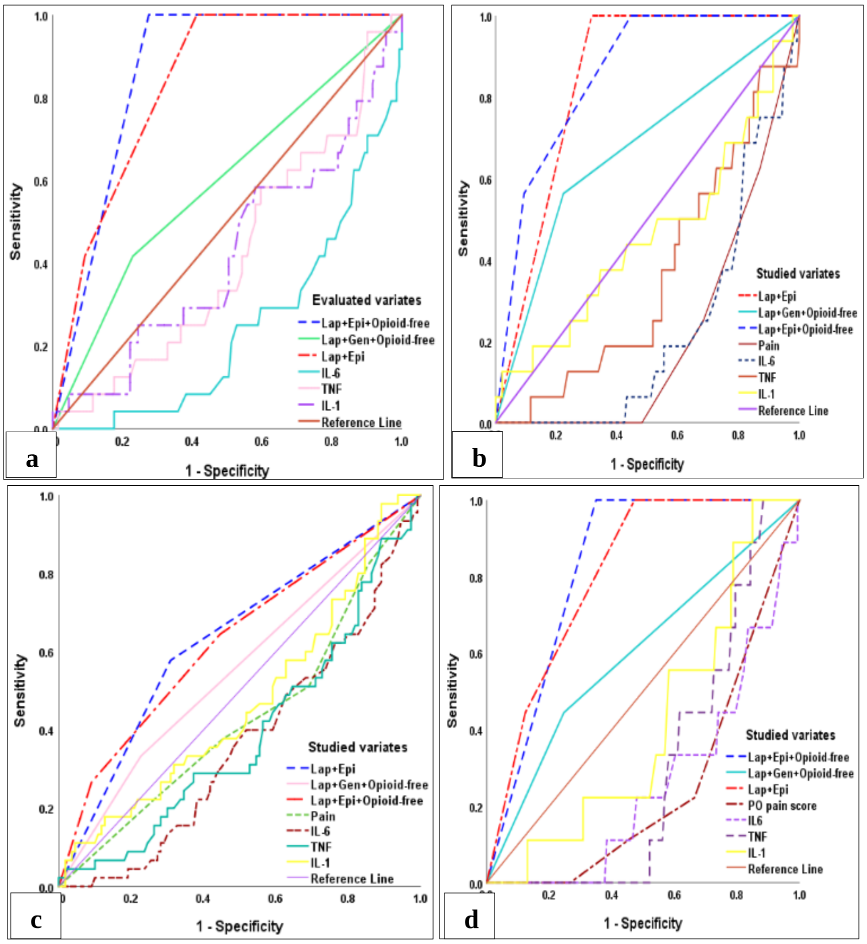

Figure 5: ROC curve for the predictors of (a) low PO pain scores, (b) short PO duration till 1st ambulation, (c) short PO duration till 1st passage of flatus, and (d) PO duration of hospital stay.

DISCUSSION

The obtained results assured the study hypothesis that laparoscopic surgery is more beneficial as regards operative and PO outcomes of patients underwent LC in comparison to OC. These beneficial outcomes were manifested as significantly lower amount of operative bleeding and shorter operative time with lower frequency of patients required ICU and shorter duration of ICU stay. Postoperatively, laparoscopy provided lower pain scores with shorter PO duration till 1st ambulation and passage of flatus and shorter duration of PO hospital stay.

In line with the study hypothesis and the obtained results, van den Brink et al reported favorable PO outcomes for colorectal laparoscopic surgery with no significant differences in total cost between laparoscopic and open colorectal surgery.[7] Also, Silinsky et al in comparison of OC versus LC reported significantly reduced opioid consumption, PO pain scores, shorter times to 1st bowel sound, 1st flatus and 1st bowel movement and length of hospital stay with decreased frequency of PO nausea and vomiting.[8] Moreover, Horie et al evaluated the feasibility of LC for patients older than 75 years and found laparoscopy is an acceptable surgical approach in these patients with higher overall survival than open approach, despite of the insignificant difference.[9] Furthermore, Huynh et al found laparoscopic approach improved the survival and recurrence rates in colonic tumors invading adjacent organs or requiring multivisceral resections in comparison to open surgical approach.[10] Additionally, Magouliotis et al reported that laparoscopic complete mesocolic excision with central vascular ligation right hemicolectomy offered advantageous short-term outcomes compared to open procedure.[11] Also, Faisal et al detected a significantly higher number of cells stained for inflammatory cytokines in patients who had open than laparoscopic colorectal resection.[12]

Thereafter, Grieco et al documented that LC with an enhanced intraoperative procedure in the form of intracorporeal anastomosis and ERAS perioperative protocol guarantee better results with lower surgical complications and faster PO recovery.[13] Dehghani et al prospectively documented that early mobilization is easy and can be implemented safely after laparoscopic surgeries and Cheng et al reported significant beneficial impacts of laparoscopic versus open splenic flexure colon cancer surgery in the form of significantly lower volume of IO blood loss, significantly shorter time to an oral diet and hospital stay, and lower PO complications.[14,15]

The reported shift of laparoscopic to open procedure (6.25%) was better than that reported by Linhares Mota et al who reported shift-to-open rate after video-laparoscopic colorectal surgery performed by residents of 23%, but was lower than the shift-to-open rate (4.8%) reported by Miljan et al.[16,17]

In support of the efficacy and improved PO outcomes of laparoscopic colonic surgery, Nozawa et al revised the randomized controlled trials investigating laparoscopic versus open proctocolectomy with ileal pouch-anal anastomosis for ulcerative colitis or familial adenomatous polyposis and reported highly significant reduction of the volume IO blood loss and laparoscopy provided shorter time to the 1st bowel movement.[18] Also, Gilna et al documented that LC for Crohn's disease in pediatric patients is safe and is associated with shorter hospital stay compared to the open procedure and with equivalent hospital costs.[19] Moreover, Smyth et al found application of laparoscopy for emergency cases presenting with intestinal obstruction, perforation and peritonitis, and for cases undergoing right hemicolectomy was associated with reduced length of stay and 30-day mortality for cases completed laparoscopically than cases converted or started with open surgery.[20] Further, Kudou et al reported that laparoscopy for colorectal perforation in an emergency setting provided significantly lower IO blood loss and surgical site infection rate than with open surgery.[21]

Further, LC effectively mitigated the surgical immune response as manifested by significantly lower serum cytokines' levels in immediate PO samples of patients had laparoscopy in comparison to levels estimated in samples of patients had OC. Moreover, at 1-week PO, the serum cytokines' levels were significantly lower than in immediate PO samples with significant difference between levels estimated in samples of patients had LC versus OC.

Similarly, Xu et al reported significantly lower levels of immune markers in samples of patients underwent laparoscopic than those had OC.[22] Also, Bohne et al reviewed 20 randomized clinical trials comparing LC versus OC and reported significantly lower serum IL-8 levels at 0-2 h after surgery and serum levels of CRP, IL-6, IL-8 and TNFα at 3-9 h after surgery in samples of LC versus OC.[23] Bohne et al in a meta-analysis of the results of 14 trials detected lower inflammation and less immunosuppression with higher innate and adaptive cell counts, higher NK cell activity at day-4 and day-8 PO after laparoscopic colectomy than after open colectomy.[24] Retrospectively, Liu et al detected significantly higher serum levels of CRP, IL-6 and TNF-α in samples of all patients at 24-hour PO in comparison to preoperative levels, but levels estimated in samples of patients had LC than that of patients had OC.[25]

In support of the favorable effect of laparoscopy on the surgical immune response, Erginel et al reported that laparoscopic appendectomy is associated with a smaller inflammatory response caused by surgical stress than open appendectomy with a significant difference between both groups as regards serum levels of soluble urokinase-type plasminogen activator receptor.[26] Also, Duan et al found laparoscopic appendectomy significantly reduced PO inflammatory factors and immune markers with significant reduction of levels of CD28 and B7H3, which is a costimulatory molecule that plays a crucial role in immune regulation.[27] Moreover, Chen et al documented that laparoscopy for early-stage endometrial carcinoma effectively reduced serum tumor marker levels, attenuated the inflammatory response and damage to immune function.[28]

Interestingly, in addition to the effect of laparoscopy, patients had LC under EA had lower serum cytokines' levels than those had LC under GA and among those had laparoscopy under GA, patients received opioid-free GA had lower cytokines' levels than patients received opioid-based general anesthesia. These results indicated the efficacy of laparoscopic surgery under epidural anesthesia especially if received non-opioid analgesia for control on surgical immune stress. In support of this assumption, statistical analyses defined laparoscopic surgery under epidural anesthesia and non-opioid analgesia as the highly significant predictor for favorable PO surgical outcomes and proper control on surgical immune response. These outcomes support the previously reported by Wang et al who found the combination of opioid-free total intravenous anesthesia (TIVA) and thoracic EA may attenuate the intraoperative stress response and PO pain in patients undergoing radical esophagectomy than TIVA alone.[29] Also, Okuda et al detected lower plasma concentrations of TNF-α and IL-6 with epidural than opioid-based TIVA and concluded that EA could attenuate local inflammatory responses to surgery.[30] Also, Jiang et al detected significantly higher levels of IL-6, IL-8, and TNF-α in sera of patients who received GA than in patients who received combined general and epidural anesthesia.[31] Regarding the opioid-free analgesia, the reported results go in hand with Titon et al who detected significant perioperative reduction of serum levels of IL-12 and TNF-α for 48-hour in patients received opioid-free than patients who received opioid-based anesthesia and concluded that opioids trigger changes in inflammatory cytokine release.[32]

Limitations

Estimation of serum levels of anti-inflammatory cytokines is a study limitation for proper evaluation of immune balance during colectomy.

CONCLUSION

Laparoscopic colectomy significantly improved PO surgical outcomes in comparison to OC. Laparoscopic surgery attenuated the surgical immune response with significant difference than open surgery. Anesthesia was found to be another determinant factor and epidural anesthesia juxtaposed with opioid-free analgesia significantly provided further control on the surgical immune response.

Recommendations

Wider scale multicenter studies are required to establish the obtained results and estimation of anti-inflammatory cytokines' levels.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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