Original Article

Can intraoperative hyperlactatemia have an impact on early postoperative infections in patients undergoing laparoscopic colorectal cancer surgery?

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ABSTRACT

Introduction: The impact of major surgery on tissue hypoxia can be evaluated indirectly with lactate at the end of the operation. This study aimed to investigate the impact of hyperlactatemia on early postoperative infectious complications at the end of surgery.

Materials and Methods: We retrospectively examined 75 patients who underwent laparoscopic resection for colorectal cancer (CRC). Lactate levels above 2 mm/L was defined as hyperlactatemia at the end of the surgery. Postoperative infectious complications occurred within the first 30 days were included in the study. The patients were divided into two groups as those with and without postoperative infection (POI).

Results: Nineteen patients (25.3%) had early POI complications. Patients in the POI group had a significant association with the Charlson Comorbidity Index (CCI) ≥3 (p=0.021) and type 2 diabetes mellitus (DM) (p=0.003). Hyperlactatemia was found to significsantly affect POI (p=0.013). Lactate levels increased in 16 (84.2%) of 19 POI patients. While the median value for the hospital stay was 7 days for those without POI, it was 11 days for those with POI (p=0.002). There was a significant relationship between general surgery site infection l (SSI) and diabetes mellitus (p=0.006), and length of hospital stay (p=0.001).

Conclusion: In this study, CCI ≥3, type 2 DM, and hyperlactatemia at the end of the operation were independent risk factors for POI in laparoscopic colorectal cancer surgery patients. SSI and POI may predict the prolonged hospital stay. To validate these findings, studies with a higher patient volume in a prospective design are required.

Keywords: Colorectal cancer; hyperlactatemia; infections; lactate.

Introduction

Despite all prevention efforts, colorectal cancer (CRC) continues to retain its potential to stay ahead in prevalence. CRC is the third most commonly diagnosed cancer worldwide and the second in terms of cancer-related deaths.[1]

Surgical treatment remains the primary treatment option. Patients who have undergone colorectal surgery for any reason can develop postoperative complications in up to 1/3 of the patients. The overall surgical site infection (SSI) is 9.4%. The rate of anastomotic leakage is between 3% and 10%.[2, 3] Pulmonary infection rate after colectomy is 6.2%.[4] After the use of laparoscopy became widespread, CRC closely followed these technological developments. Nowadays, due to its many advantages, such as short hospitalization, better cosmetics, less incisional hernia, etc. the laparoscopic approach is preferred by many clinics without neglecting oncological results.[5] It was reported that laparoscopic colorectal surgery reduced SSI in a meta-analysis involving 5797 patients, including sixteen randomized controlled trials.[6] Besides, the positive effects of laparoscopy on hospital stay were accepted by everyone.

Prolonged operative time, such as cancer surgery, may increase lactate levels secondary to tissue hypoperfusion. An increased intraabdominal pressure (IAP) in laparoscopy reduces splanchnic blood flow and impairs tissue perfusion.[7] In addition, an IAP increase also reduces hepatic and renal blood flow, which are the elimination organs of lactate.[8] As a result of all these effects, laparoscopic surgery may be associated with increased lactate levels.

The decrease in oxygen support and tissue hypoxia due to microvascular flow impairment underlies the complications after major surgery. Lactate is an essential marker of hypoperfusion.[9] The effect of major surgery on tissue hypoxia can be indirectly evaluated with lactate at the end of the operation.[10]

Many studies in the literature highlight the prognostic importance of hyperlactatemia.[11] We hypothesize that intraoperative hyperlactatemia may affect early postoperative infective outcomes.

Our aim in this study was to investigate the effect of hyperlactatemia at the end of surgery on early postoperative infectious complications.

Materials and Methods

Ethical approval (Ethical Committee No. 2019.4/23-200) was provided by the Institutional Research and Ethics Committee of our hospital. This committee waived the need for informed consent from all eligible patients.

We retrospectively enrolled 75 patients who underwent laparoscopic resection for colorectal cancer in our center between January 2013 and June 2019. In this study, exclusion criteria were emergency surgery or palliative surgery, under 18 years of age, and conversion to open surgery. Initial lactate levels were determined from blood gas analysis before the incision. The end lactate values were recorded at the completion of the operation. Patients, those who had an initial intra-arterial blood lactate level higher than 2 mmol/L, were excluded from the analysis. Patients with chronic kidney, liver, and heart disease with impaired organ function were also excluded from the study. Hyperlactatemia defined as lactate levels exceed 2 mm/L at the end of the surgery.[12] Postoperative infectious complications within the first 30 days were included in this study. These were pulmonary, urinary tract, and central-venous-catheter-related bloodstream infections. Incisional SSI (superficial and deep) and organ-space SSI, such as anastomotic leak and intraabdominal abscess, were also recorded. The patients were divided into two groups as those with and without postoperative infection (POI).

Standard anesthesia induction was applied to all patients with 1−2 mcg/kg fentanyl, 2 mg/kg propofol, and 0.1 mg/kg rocuronium. Maintenance of the sevoflurane dose was adjusted with the Bispectral Index (BIS) monitoring in the range of 0.8−1 minimum alveolar concentration (MAC). We performed rectal cancer surgery partially in the Trendelenburg position. The pneumoperitoneum pressure of the patients was adjusted as 12−14 mmHg.

The demographic, clinical, and surgical characteristics of the patients were included in the study. The variables were age, sex, Charlson comorbidity index (CCI),[13] American Society of Anesthesiologists (ASA) score, BMI, type 2 diabetes mellitus (DM), hyperlactatemia, tumor localization, tumor size, TNM stage, and length of hospital stay. Operative details included total volume of administered fluids, the volume of urine output, the volume of blood loss, and surgery time.

Statistical Analysis

The SPSS (Statistical Product and Service Solutions) software version 22 for Windows (SPSS Inc. Chicago, IL, USA) was used for statistical analyses of the study. The

normality of the distribution of the data was carried out using the Kolmogorov-Smirnov test. Qualitative data were presented as frequency and percentage. Quantitative data were given as mean±SD if the data were normally distributed, and median (Interquartile Range-IQR) if not normally distributed. The association of postoperative infective complications with categorical variables was analyzed using Chi-square and Fisher's exact tests. The Mann-Whitney-U test was used to examine whether postoperative infections were related to blood loss, administered fluid volume, urine output, and length of hospital stay. The effect of operative time on postoperative infective complications was investigated with the student's t-test. A p-value lower than 0.05 was accepted as statistically significant.

Results

Of the 75 patients, 19 (25.3%) had early postoperative infective complications. Table 1 shows the demographic, clinical, and surgical characteristics of patients. The median age of the POI group was 62 (56−72), while the other group without infection was 60 (50−66). Seven out of 24 elderly patients struggle with an infection after the operation (p=0.601). In the infective group, the female-male ratio was very close to each other (p=0.943). It was observed that patients in the infective group had a significant association with CCI ≥3 (p=0.021). Eight (42.1%) of these 19 patients with POI had Type 2 DM, and this was a facilitating factor for POI (p=0.003). Another parameter in this study that had a significant relationship with POI and affected it was hyperlactatemia (p=0.013). Lactate levels were elevated in 16 (84.2%) of 19 POI patients. Those without POI stayed in the hospital for 7 days as the median value, while those with POI stayed for 11 days (p=0.002). There was no significant association between the other variables included in the study and POI.

Table 2 shows the types of postoperative infections in patients with hyperlactatemia. The most common of these complications was incisional SSI, and it affected 5 of the 16 patients. The incidence of incisional SSI in all patients was 6.6%. Three patients with anastomotic leak followed this complication. One patient had to undergo a percutaneous procedure due to intraabdominal abscess. The incidence of organ/space SSI was 8.0%, and the overall SSI was 12.0%. Pulmonary infections were also observed in three patients. Urinary tract infection and central-venous-

catheter-related bloodstream infections were detected in two patients in both.

Table 3 shows the significant relationship between overall SSI and diabetes mellitus (p=0.006) and length of hospital stay (p=0.001).

Discussion

In this study, we aimed to investigate the effect of intraoperative hyperlactatemia on early postoperative infective complications based on a retrospective analysis of a total of 75 patients who had laparoscopic surgery due to colorectal cancer. Our results showed that increased Charlson comorbidity index (CCI ≥3), type II DM, and hyperlactatemia were a significant risk factor for infections in the early postoperative period. It was also found that patients with POI had prolonged hospital stays.

So far, many studies have been conducted with risk factors for CRC complications. It is possible to collect all of these in the subgroup related to the patient, the disease, and the operation. Examples include advanced age, male gender, high ASA score and CCI, prolonged operation time, high blood loss, advanced cancer stage.[2] It is possible to increase the numbers of these variables. Many of the parameters that facilitate this infection are associated with impaired oxygen delivery to the tissue. Hypoxic conditions cause a series of chains of events in which lactate plays a vital role. Bakker et al.[14] reported that high CCI is a risk factor for an anastomotic leak. In those with comorbidity, pulmonary (6.2%) and urinary tract infection (5%) were the most frequent complications.[15] Similar results for overall infectious complications in high CCI status were also valid in our study.

Laparoscopic surgery is a minimally invasive procedure, and it is associated with less SSI compared to conventional surgery. The incidence of incisional SSI ranges from 3.3%[16] to 26%.[17] Poon et al.[18] reported the organ/space SSI incidence rate as 2.7%. The overall incisional and organ/space SSI rate in our study was 12.0%, 6.6%, and 5.3%, respectively. It was compatible with the literature. Operative factors for the SSI are more critical than patient factors.[16]

Diabetes is a generally accepted risk factor for infectious complications after surgery.[19] DM was also found to be closely related to SSI.[20] In our study, type 2 DM, similar to most literature results, was in a significant association with both overall infection and SSI.

Table 1. Demographic, clinical, and surgical characteristics of the patients

Variables	Total patients (n=75)				
	Postoperative infection (POI)				
	No (n=56) (74.7%)		Yes (n=19) (25.3%)		
	n	%	n	%	p
[a]Age, 65 years					
<65	39	69.6	12	63.2	0.601
≥65	17	30.4	7	36.8	
[a]Sex					
Male	30	53.6	10	52.6	0.943
Female	26	46.4	9	47.4	
[a]BMI kg/m^2					
<30	39	69.6	10	52.6	0.178
≥30	17	30.4	9	47.4	
[a]CCI					
<3	40	71.4	8	42.1	**0.021**
≥3	16	28.6	11	57.9	
[a]ASA score					
I-II	26	46.4	5	26.3	0.124
III-IV	30	53.6	14	73.7	
[b]Type 2 DM					
No	51	91.1	11	57.9	**0.003**
Yes	5	8.9	8	42.1	
[b]Localization					
Colon	41	73.2	15	78.9	0.765
Rectum	15	26.8	4	21.1	
[a]Tumor size					
<5cm	45	80.4	15	78.9	>0.999
≥5cm	11	19.6	4	21.1	
[a]Hyperlactatemia					
No	27	48.2	3	15.8	**0.013**
Yes	29	51.8	16	84.2	
[a]TNM stage					
I-II	35	62.5	13	68.4%	0.621
III-IV	21	37.5	6	31.6%	
	Mean±SD or Median (IQR)				
[c]Operative time/min	208±55		216±68		0.605
[d]Blood loss/mL	50 (40−100)		75 (50−150)		0.162
[d]Administered Crystalloid /mL	2000 (1500−2900)		2000 (1500−3000)		0.932
[d]Urine output/mL-h	50 (45−65)		55 (50−70)		0.224
[d]Length of hospital stay/day	7 (6−8)		11 (7−14)		0.002

[a]Chi-Square test; [b]Fisher's exact test; [c]Student t test; [d]Mann-Whitney U test; SD: Standart deviation; POI: Postoperative infection; BMI: Body mass index; CCI: Charlson comorbidity index; ASA: American society of anesthesiologists; DM: Diabetes mellitus.

Table 2. Types of postoperative infections in patients with hyperlactatemia

POI and Hyperlactatemia	
Type of the POI	**n=16**
Incisional SSI	5
Anastomotic leak	3
Pulmonary infection	3
Urinary tract infection	2
Central-venous-catheter-related bloodstream infection	2
Intra-abdominal abscess	1

POI: Postoperative infection; SSI: Surgical site infection

Hyperlactatemia, defined by blood lactate level>2, is an important key to sepsis and shock.[21] Lactate can predict complications as an indirect tissue hypoxia marker. [9] Any major surgical procedure triggers a series of reaction chains by stimulating neuroendocrine and inflammatory responses and then leads to an increase in tissue oxygen consumption. Adequate oxygen delivery is essential in anastomosis in colorectal surgery. Challenge and extended interventions such as cancer surgery and increased IAP in laparoscopy can increase lactate values and decrease intestinal blood flow by causing hypoperfusion in the splanchnic area. These conditions can also endanger anastomosis.[22–24] Also, increased IAP with pneumoperitoneum leads to reduced blood flow of the liver and kidneys, which prevents lactate from being excreted from the body.[7] Thus, hyperlactatemia can be seen in laparoscopic colorectal cancer surgery.

Colorectal surgery has four times increased SSI compared

to other abdominal procedures.[19] In the review of An et al.,[25] patients with colorectal resection by laparoscopic approach had increased hospitalization times compared to those without SSI.

Yates et al.[22] reported that elevated lactate values at postoperative 3rd hour independently predicted major complications and prolonged length of hospital stay. According to the results of this present study, those with POI and SSI were related to extended stays in the hospital.

This study had some limitations. The retrospective model and the relatively small patient volume were the leading ones.

Conclusions

In this study, conducted in patients with laparoscopic colorectal cancer surgery, CCI ≥3, type 2 DM, and hyperlactatemia at the end of the operation were independent risk factors for POI. POI and SSI may predict the prolonged length of hospital stay. To confirm these outcomes, high volume studies in the prospective design are required.

Disclosures

Ethichs Committee Approval: Ethical approval (Ethical Committee No. 2019.4/23-200) was provided by the Institutional Research and Ethics Committee of our hospital. This committee waived the need for informed consent from all eligible patients.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Table 3. Relationship between overall SSI and diabetes mellitus and length of hospital stay

	Overall SSI (n=9)				p
	No		**Yes**		
	n	**%**	**n**	**%**	
[a]Diabetes mellitus					
No	58	87.9	4	44.4	**0.006**
Yes	8	12.1	5	55.6	
[b]Length of hospital stay/day	66		9		**0.001**

[a]Fisher's exact test; SSI: Surgical site infection.

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