Predictive factors of postoperative paralytic ileus following abdominal surgery: a clinical study

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Abstract

Background: Post-operative ileus is a surgical complication caused by impairment in the gastrointestinal motility with incidence range from 10 to 30%. The exact pathophysiology is not well understood although many authors suggested multifactorial relations that include surgical stress response electrolyte imbalances, and fluid overload.

Objectives: to assess the risk factors associated with post-operative ileus, the technique of rapid diagnosis and management strategies and the overall progress of the patient. Methods: a retrospective study was conducted from March 2019 to January 2020 on 499 patients who underwent abdominal surgery at two tertiary hospitals in the Taif city, Saudi Arabia. The data included baseline patient characteristics, history of previous surgeries, ASA classification, operative characteristics and postoperative outcomes and care patients received.

Results: The findings showed that incidence of post-operative ileus was 12.4%. It was found that BMI>25, cardiac diseases, history of previous abdominal surgery, chemotherapy, decreased preoperative albumin levels, surgeries involving gastrointestinal are a postoperative hypokalemia, and increased hospital stay >3 days were found to be independent risk factors for post-operative ileus.

Conclusion: Identification of risk factors of paralytic ileus before surgery not only helps to assess the surgical risk, but also helps in improving the post-operative management. This will in turn reduce the incidence of post-operative ileus.

Keywords: predictive, postoperative, ileus, abdominal, surgery, Taif

Introduction

Patients who have had abdominal surgeries, particularly colon and rectal surgeries, are at risk for developing post-operative ileus (POI), a surgical complication that impairs gastrointestinal (GI) motility (1).

Between 10% and 30% of patients who undergo abdominal surgery develop POI (2). According to the systematic review of Wolthuis et al and meta-analysis of randomized control trials, individuals who underwent abdominal surgery had an incidence of 10.2% (3). The precise pathophysiology of POI is not fully understood, despite the fact that many authors have suggested multifactorial relationships that include surgical stress response manifested as spinal-intestinal neural reflexes, agonism of gut opioid receptors brought on by opiate use, sympathetic hyperactivity, electrolyte imbalances, and fluid overload that worsens the condition (4,5).

Researchers have found a number of predictors and risk factors for POI in patients who had colon and rectal surgery. Evidence suggests that factors such as advancing age, operating difficulty (type), length of surgery, decline in pre-to-postoperative hemoglobin, use of opioids for a longer period of time, use of nasogastric drainage for a longer period of time, excessive surgical bowel handling, etc (6,7,8).

The sympathetic nervous system, which is typically inhibitory to the gastrointestinal tract during the postoperative period, becomes hyperactive and contributes to POI (9,10). Longer hospital stays are linked to an increased risk of other complications, such as nosocomial infections, hernia formation, slowed healing, and wound dehiscence, as well as pulmonary thromboembolic complications and higher postoperative mortality. POI has significant financial effects on patients as well as the healthcare system (11).

The incidence of postoperative ileus normally varies by procedure type, peaking in abdominal surgery at between 9.1 and 10.4% of all surgical patients and being lowest in orthopedic surgery at around 2.1% (3).

There is very limited data available regarding the incidence of POI and so far no prospective studies have been conducted in the Kingdom of Saudi Arabia. From a clinical perspective, there is still a need to identify and predict patients who are at risk of developing postoperative ileus. Thus, this study aimed to analyze the incidence and risk factors associated with POI in patients who underwent surgeries related to the abdomen.

Subjects and Methods

Study design, location and time frame: a retrospective analytical observational study was conducted at King Abdulaziz Specialist Hospital and King Faisal Medical Complex in Taif city, Saudi Arabia from March 2019 to January 2020.

Study participants: The study included 499 patients. The inclusion criteria were adults aged more than 18 years who had undergone surgeries related to the abdomen. The exclusion criteria were patients having surgeries related to other sites and patients who had confirmed anastomotic leak, peritonitis or abdominal abscess, as these complications can have a confounding bias in the association of causation of POI.

Data collection: Data was retrieved from the database of the two hospitals. A pre-designed checklist was prepared to collect data about baseline patient characteristics (sociodemographic, body mass index, smoking status and other co-morbidities), history of previous surgeries, ASA classification, factors related to and type of surgery performed, operative characteristics, medical management and postoperative outcomes and care patients received. The incidence rate of POI was recorded if two or more of the following factors [a) nausea or vomiting, b) inability to tolerate an oral diet over the last 24 hours, c) absence of flatus over the last 24 hours, d) abdominal distension, e) radiologic confirmation] were present on or after the 4th day of surgery. For the aim of ruling out an intestinal obstruction, a plain radiography of the abdominal cavity in the supine and upright views was performed in all patients with signs of POI.

Ethical considerations: The research was approved by Research Ethics Committee of Research and Studies Department, Directorate of Health Affairs Taif (approval letter number 222 and date 7-4-2019). The confidentiality of participants was preserved by not including their names or any details that may identify them.

Data analysis: Data collected were entered and tabulated in Microsoft Excel first and transferred to SPSS Ver. 23 for statistical analysis. An independent statistician carried out statistical analysis. We used numerical figures and percentages for categorical variables and Pearson's Chi-Square test ($\chi 2$) or Fisher's exact test was used to compare them. Continuous variables were measured using mean and standard deviation and comparisons were done using the student's t-test. Multivariate analysis was performed to identify predictive factors for POI and variables that showed statistical significance ($p<0.05$) were entered into the logistic regression model for multivariate analysis. Odd's ratio (OR) at 95% confidence interval was calculated for each variable and those that showed statistical significance ($p<0.05$) showing an OR>1, were predicted as independent risk factors for POI.

Results

Our prospective study included 288 male and 211 female patients with a mean age of 42.6 ± 19.5 years. The incidence rate of POI was 12.4% (n=62) and the rate was comparatively more in females than males (p<0.05), Of whom, 45.5% had one or more systemic diseases, with pulmonary diseases the most common comorbidity (8.2% (n=41)).

Table 1 shows the comparison of socio-demographic characteristics between POI and non-POI patients. It was found that POI patients had a significantly higher percent of those of older age above 65 years, had a history of previous surgery, had class 3 or more category on the ASA Physical Status classification system, and were chronic users of steroids (P=< 0.05). At the same time, POI patients had a significantly higher percentage of having chemotherapy and having lower pre-operative albumin levels (1.80 ±0.40 g/dL vs. 1.98 ±0.23) g/dL (p=< 0.05).

Table 2 shows the comparison of operative and post-operative variables between the two groups. The most common type of surgery performed in our study population was gastrointestinal (GIT) related (84.3%) surgeries. The incidence of POI was statistically higher in patients who underwent GIT surgery, and who had emergency surgeries (p=< 0.05). A non-significant relationship was found between the two groups according to the post-operative blood parameters including sodium levels (p=<0.05).

POI group had a significant longer duration of operation (108 ± 59.1 min. vs. 100±54.3), and a higher percentage of staying in hospital more than 72 hours (p=< 0.05).

The univariate logistic regression analysis showed that female gender, age >65 years, BMI>25, cardiac diseases, type 2 Diabetes Mellitus, hypertension, history of previous abdominal surgery, ASA class>3, chronic use of steroids, history of chemotherapy, hypoalbuminemia, surgeries of GIT, appendectomy, emergency surgery, post-operative parameters like Hyponatremia, hypokalemia, Hyperchloremia and patients who stayed in the hospital for more than 72 hours were potential predictive factors of POI (Table 3).

Subsequent multivariate logistic regression showed that BMI>25 [OR 2.07, 95% CI 1.24-3.47, p=0.006], Cardiac disease [OR 7.98, 95% CI 1.46-43.75, p=0.017], history of previous surgery [OR 1.89, 95% CI 1.07-3.32, p=0.028], ASA class>3 [OR 2.34, 95% CI 1.12-4.58, p=0.013], history of chemotherapy [OR 370.4, 95% CI 33.3-5802.4, p<0.001], preoperative hypoalbuminemia [OR 4.02, 95% CI 1.81-8.91, p=0.001], GIT surgery [OR 6.45, 95% CI 2.04-20.35, p=0.001], emergency surgery [OR 2.64, 95% CI 1.47-4.75, p<0.001], postoperative hypokalemia [OR 2.38, 95% CI 1.04-4.22, p=0.010] and postoperative length of stay more than 72 hours [OR 2.73, 95% CI 1.63-4.60, p<0.001] were independent predictive factors for POI (Table 3).

In our study 96.7% of cases with POI resolved with conservative measures with a median duration for POI of 4.5 days.

Table 1: Comparison of socio-demographic characteristics between the groups

Variables	Group of Patients		*P value* *
	POI	Non-POI	
Gender (Female/Male)	32/30	160/277	0.002
Age (≤65 years / >65 years)	45/17	406/31	<0.001
BMI (≤25 / >25)	25/37	279/158	<0.001
Smoking history	8 (12.9%)	124(28.3%)	<0.001
Chronic diseases	26 (41.9%)	285(65.2%)	<0.001
Pulmonary disease	6 (9.67%)	35 (8%)	0.605
Cardiac diseases	4 (6.45%)	3(0.7%)	<0.001
Diabetes Mellitus	19 (30.6%)	65(14.8%)	<0.001
Hypertension	16 (25.8%)	79 (18.1%)	0.023
Previous surgery	33 (53.2%)	127 (29.1%)	<0.001
Previous paralytic ileus	2(3.2%)	5(1.1%)	0.580
ASA status (>class 3)	20 (32.25%)	50 (11.4%)	<0.001
Chronic use of opioids	5(8.1%)	29 (6.6%)	0.615
Chronic use of steroids	3 (4.8%)	6 (1.4%)	0.017
Antibiotic use	10 (16.1%)	88 (20.1%)	0.218
Chemotherapy	3 (4.8%)	1(0.2%)	<0.001
Pre-operative albumin	1.80 (1.74-1.85)	1.98(1.97-2.0)	<0.001

* p<0.05 is considered as statistically significant; * BMI = Body Mass Index, ASA= American Society of Anesthesiologists Physical Status classification system,

Table 2: Comparison of operative characteristics between the groups

Variables		Group of Patients		*P value**
		POI	Non-POI	
Type of surgery	Bariatric	2 (3.2%)	4(0.9%)	0.093
	Colorectal	3 (4.8%)	45 (10.3%)	0.028
	GIT	57 (91.9%)	364 (83.2%)	0.003
	OBG/GYN	0 (0%)	24(5.5%)	<0.001
Nature of surgery	Emergency	37 (59.6%)	200(45.7%)	<0.001
	Elective	25 (30.4%)	237 (54.3%)	<0.001
Post-operative blood parameters	Estimated Blood Loss (ml)	177.7 (135.8-219.4)	209.39 (160.4-258.3)	0.109
	Postoperative hemoglobin level (g/dL)	26.19 (20.7-31.7)	20.4 (16.9-23.9)	<0.001
	Postoperative Sodium level (mEq/L)	138.7 (138.1-139.3)	138.6 (138.2-138.9)	<0.001
	Postoperative potassium level (mmol/l)	3.89 (3.80-3.95)	4.48 (4.02-4.95)	0.060
	Postoperative Chlorine level(mEq/L)	105.3 (104.5-105.9)	102.7 (101.5-103.9)	0.342
Length of operation (minutes)		108.5(100.3-116.7)	100.1(93.9-106.3)	0.045
Wound infection		3 (4.8%)	41 (9.4%)	0.287
Sepsis		0(0%)	6 (1.3%)	0.098
Length of stay >3days)		31 (50 %)	106 (24.2%)	<0.001

*p<0.05 is considered as statistically significant
*GIT= Gastrointestinal, OBG/GYN= Obstetrics and gynecology

Table 3: Logistic regression analysis of Predictive risk factors of Postoperative ileus

	Univariate analysis				Multivariate analysis			
Variables	OR	95% CI		*P value**	OR	95% CI		*P value**
		Lower	Upper			Lower	Upper	
Female Gender	1.76	1.22	2.53	0.002	1.52	0.87	2.36	0.375
Age (≤65 years / >65 years)	5.21	2.97	9.12	<0.001	1.63	0.63	4.20	0.312
BMI (≤25 / >25)	2.49	1.73	3.60	<0.001	2.07	1.24	3.47	0.006
Smoking history	0.40	0.24	0.63	<0.001				
Pulmonary disease	0.85	0.45	1.60	0.605				
Cardiac diseases	10.9	2.47	48.88	<0.001	7.98	1.46	43.75	0.017
Diabetes Mellitus	2.61	1.68	4.04	<0.001	1.04	0.47	2.30	0.933
Hypertension	1.64	1.07	2.52	0.023	0.62	0.27	1.43	0.260
Previous surgery	2.82	1.94	4.09	<0.001	1.89	1.07	3.32	0.028
Previous paralytic ileus	1.48	0.37	5.99	0.580				
ASA status (>class 3)	3.67	2.31	5.83	<0.001	2.34	1.12	4.58	0.013
Chronic use of opioids	1.19	0.60	2.36	0.615				
Chronic use of steroids	3.82	1.18	12.34	0.017	2.308	0.61	11.46	0.259
Antibiotic use	0.74	0.46	1.19	0.218				
Chemotherapy	15.4	1.96	121.4	<0.001	370.4	33.3	5802.4	<0.001
Preoperative Hypoalbuminemia	6.05	3.09	11.84	<0.001	4.02	1.81	8.91	0.001
Bariatric surgery	0.27	0.05	1.39	0.12				
Colorectal surgery	0.45	0.21	0.93	0.03				
GIT surgery	2.46	1.34	4.53	<0.001	6.45	2.04	20.35	0.001
OBG/GYN surgery	0.08	0.01	0.58	0.010				
Cholecystectomy	0.57	0.32	1.01	0.06				
Appendectomy	2.28	1.47	3.53	<0.001	0.69	0.36	1.37	0.301
Emergency surgery	1.81	1.25	2.59	<0.001	2.64	1.47	4.75	0.001
Laparoscopy	0.71	0.49	1.03	0.073				
Open surgery	1.41	0.97	2.05	0.073				
Estimated Blood Loss (<500/ >500ml)	0.74	0.46	1.18	0.21				
Postoperative anemia	0.45	0.30	0.67	<0.001				
Hyponatremia	2.24	1.32	4.10	<0.001	1.04	0.43	2.51	0.918
Hypokalemia	2.14	1.39	3.33	<0.001	2.38	1.08	4.22	0.010
Hyperchloremia	3.81	1.94	7.51	<0.001	1.53	0.61	3.95	0.355
Length of operation	0.99	0.98	1.59	0.92				
Wound infection	1.69	1.69	4.44	0.29				
Length of stay >3 days	3.19	2.17	4.67	<0.001	2.73	1.63	4.60	<0.001

*p<0.05 is considered as statistically significant
*OR=Odds Ratio, BMI = Body Mass Index, ASA= American Society of Anesthesiologists Physical Status classification system, GIT= Gastrointestinal, OBG/GYN= Obstetrics and gynecology.

Discussion

Our study included a total of 499 patients who have undergone surgery related to the abdominal area in two hospitals in the city of Taif. To date there have been no studies done in the Kingdom of Saudi Arabia that assessed the predictive factors of POI. The findings of our study showed that the incidence of Postoperative ileus (POI) was 12.4%. Internationally there is a lack of standardized definition for POI and different studies have defined POI based on different diagnostic criteria and we have followed the definition suggested by Vather et al due to its wide acceptability around the world (8).

Comparing the incidence to other studies conducted in various parts of the world, it is relatively similar (3). In contrast to our analysis in various abdominal procedures, a Canadian study (12) that included 323 patients who had colon surgery revealed a 19% incidence.

The gastrointestinal motility is altered in patients with POI due to surgical stress, and the inflammatory mediators released also play a role in this pathophysiology (13).

The present work found 10 independent predictive risk factors for POI such as BMI>25, Cardiac disease, history of previous surgery, ASA class>3, history of chemotherapy, preoperative hypoalbuminemia, GIT, emergency surgery, postoperative hypokalemia and post operative length of stay more than 72 hours.

Visceral adipose tissue can deposit heavily in obese or BM1>25 individuals, which might result in surgical complications including POI (14). Visceral obesity is also clearly linked to a number of cardiovascular and metabolic co-morbidities, including type 2 diabetes mellitus, hypertension, ischemic heart disease, and stroke (15,16). Higher BMI has been found in other studies to be a predictor of POI, which is consistent with our findings (17,18). Patients having a history of prior abdominal surgery were found to have an independent risk factor for POI in our study. After surgery, GI motility is lowered because the sympathetic nervous system is more activated than the parasympathetic nervous system, and this could get worse if the patient has another surgery at the same site (19).

Increased age has been identified as an independent risk factor for POI in numerous investigations (20-23). Even while our Univariate analysis indicated that advanced age (>65 years) was a risk factor, it lost its significance when it was added in the multivariate analysis. Elderly individuals typically have less functional and nutritional deficiencies, and there may also be an imbalance in the levels of inflammatory mediators (24).

Additionally, the multivariate analysis revealed that characteristics including hypoalbuminemia and ASA>3 were independent risk factors for POI. Patients who are elderly frequently have hypoalbuminemia or other nutritional deficits and may also fall under the ASA>3 category. Therefore, the interaction of these factors may be the cause of the insignificant relationship of advanced age (20, 25, 26).

Among surgical procedures, GIT surgery was identified as a standalone risk factor for POI. In contrast to previous abdominal surgeries, total gastrectomy involves the surgical removal of the vagus (vasectomy) (27). The vagus nerve is frequently preserved during various abdominal procedures, which may facilitate a quicker recovery of gastrointestinal motility (28).

Chemotherapy was a substantial additional predicted risk factor in our analysis. Patients with any type of cancer who take chemotherapy drugs like vincristine and vinblastine or opioids may experience decreased intestinal motility (29). The toxicity of other medications that affect vincristine's metabolism can also be increased (30). Additionally, medications like opioids, which are used to treat cancer patients' pain, may sometimes spontaneously cause ileus (31, 32). Emergency surgery has worse outcomes than elective surgery, and it poses a significant risk of POI (33).

This study also showed that emergency surgery is also a separate risk factor for development of POI. The cause of this may be that patients receiving emergency abdominal surgery are frequently not adequately prepped or examined, unlike those undergoing elective surgery, and/or that other risk factors connected with it were not identified in advance due to a lack of time.

In the current study's univariate analysis, the postoperative blood parameters haemoglobin (Hb), sodium (Na+), potassium (K+), and chloride (Cl_) levels were found to be significant independent risk factors except for postoperative hypokalemia, however, which appeared as non-significant in multivariate analysis. Studies have indicated that risk factors for hypokalemia include advanced age, ASA>3, diabetes, hypertension, antihypertensive medications, diuretic drugs, laxative misuse, etc (34, 35, 36).

Although hypokalemia is linked to symptoms including mental depression, weakness, and more severe deficits result in muscle paralysis impairing gastrointestinal motility frequently leading to POI, the precise mechanism by which it causes POI is unknown (37). LOS >72 hours was the second important independent risk factor in our analysis. LOS is a significant health economic metric that depends on preoperative, surgical, and postoperative circumstances (38).

LOS >72 hours has also been linked to characteristics including advanced age, an ASA score of 3 or higher, the presence of chronic conditions, and the type of operation, among others (38, 40). According to studies, LOS has a stronger association with intraoperative and postoperative parameters than preoperative ones (41, 42).

The fact that this was a multi-center study and we evaluated approximately 33 variables is one of the study's strong points. Before interpreting our findings, it is important to take into account the study's numerous limitations.

Gender is a recognised independent risk factor for POI, according to numerous research (22, 43). However, outside of a univariate study that identified female gender as a risk factor, we did not find gender to be particularly relevant in our research. This may be because studies have shown that less severe POI has no association with gender whereas severe POI does, suggesting that the male gender association relies on the degree of the POI (44).

Limitations

One of the present study limitations was that patients were not categorized based on severity. This could be a reason for the non-significant association of gender. Having a retrospective study design encountered biases, as such it is also difficult to control the nuisance variables when conducting a retrospective hospital-based study.

Conclusion

Our study findings showed that incidence of POI was 12.4% in patients who underwent abdominal surgery. It was found that BMI>25, cardiac diseases, history of previous abdominal surgery, chemotherapy, decreased preoperative albumin levels, surgeries involving gastrointestinal area, postoperative hypokalemia, and increase hospital stay >3 days were found to be independent risk factors for POI. Prior to surgery, it is crucial that the medical team (internists, pulmonologists, cardiologists, and anesthetists, among others) identify these risk factors. This will not only assist in determining the surgical risk but also enhance postoperative care, lowering the incidence of POI.

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