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Preoperative Leukocytosis in Colorectal Cancer Patients

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Background: Preoperative asymptomatic leukocytosis has been reported as a factor that affects morbidity of surgical patients. We sought to identify the relationship between asymptomatic preoperative leukocytosis and postoperative complications in elective colorectal cancer surgery.

Study Design: The NSQIP database was used to examine the clinical data of patients who had preoperative leukocytosis (white blood cell count more than 11,000/mL) and colorectal cancer resection from 2005 to 2013. Patients with preoperative sepsis, recent steroid use, disseminated cancer, renal failure, pneumonia, and emergently admitted patients were excluded from the study. Multivariate regression analysis was performed to identify outcomes of preoperative leukocytosis.

Results: We evaluated a total of 59,805 patients with a diagnosis of colorectal cancer who underwent colorectal resection. The rate of preoperative asymptomatic leukocytosis was 5.6%. Asymptomatic leukocytosis was associated with preoperative serum albumin level (adjusted odds ratio [AOR] 0.58, $p < 0.01$) and blood urea nitrogen/creatinine ratio (AOR 1.01, $p < 0.01$). Preoperative asymptomatic leukocytosis had significant associations with increased mortality (AOR 1.76, $p < 0.01$) and morbidity of patients (AOR 1.26, $p < 0.01$). Postsurgical complications that had the strongest associations with asymptomatic leukocytosis were cardiac arrest (AOR 1.78, p ¼ 0.03) and unplanned intubation (AOR 1.61, $p < 0.01$). Also, infectious complications were significantly higher in patients with leukocytosis (AOR 1.18, p ¼ 0.01).

Conclusions: Preoperative asymptomatic leukocytosis has a prevalence of 5.6% in colorectal cancer resections and carries a significant increased risk of mortality and morbidity. Asymptomatic leukocytosis is associated with preoperative dehydration and malnutrition. Further studies are indicated to validate and explain these findings.

Colorectal cancer is the third most common malignant neoplasm worldwide, and is the second leading cause of cancer deaths in the United States.[1,2] Although treatment of colorectal cancer has improved over the past 2 to 3 decades, we still need a better understanding of the role of the host response to malignancy, possible paraneoplastic syndromes, and better identification of potential prognostic predictors.

Numerous biomarkers have been introduced as prognosis predictors for colorectal cancer.3 Recent advances indicate biomarkers may herald the next major advancement in the treatment of colorectal cancer.[3] Colony-stimulating factors (CSFs) are well-known biomarkers responsible for the in vitro and in vivo proliferation of bone narrow progenitor cells into mature differentiated cells.[4] Presence of CSF receptors has been reported in lung, ovarian, and bladder malignant tumors and can be associated with

asymptomatic leukocytosis.[5-8] Presence of receptors of CSFs in colorectal malignant tumors has been reported in the literature as well.[4] In lung cancer, tumor-related leukocytosis has been reported as a poor prognosis factor that has a link with the expression of CSF biomarkers.[9,10] This link between baseline elevated leukocyte count due to expression of the CSF biomarkers and lung cancer is well established, but has not been explored for colorectal cancer.[9,10] A large nationwide study investigating asymptomatic leukocytosis in colorectal cancer patients is of interest. This study aimed to investigate the incidence and report outcomes of asymptomatic leukocytosis in colorectal cancer patients who underwent colorectal resection, and provide a more in-depth analysis of the relationship between leukocytosis and colorectal cancer patient outcomes.

Abbreviations and Acronyms

AOR	=	adjusted odds ratio
BUN/Cr	=	serum blood urea nitrogen/serum creatinine ratio
CSF	=	colony-stimulating factor
SSI	=	surgical site infection

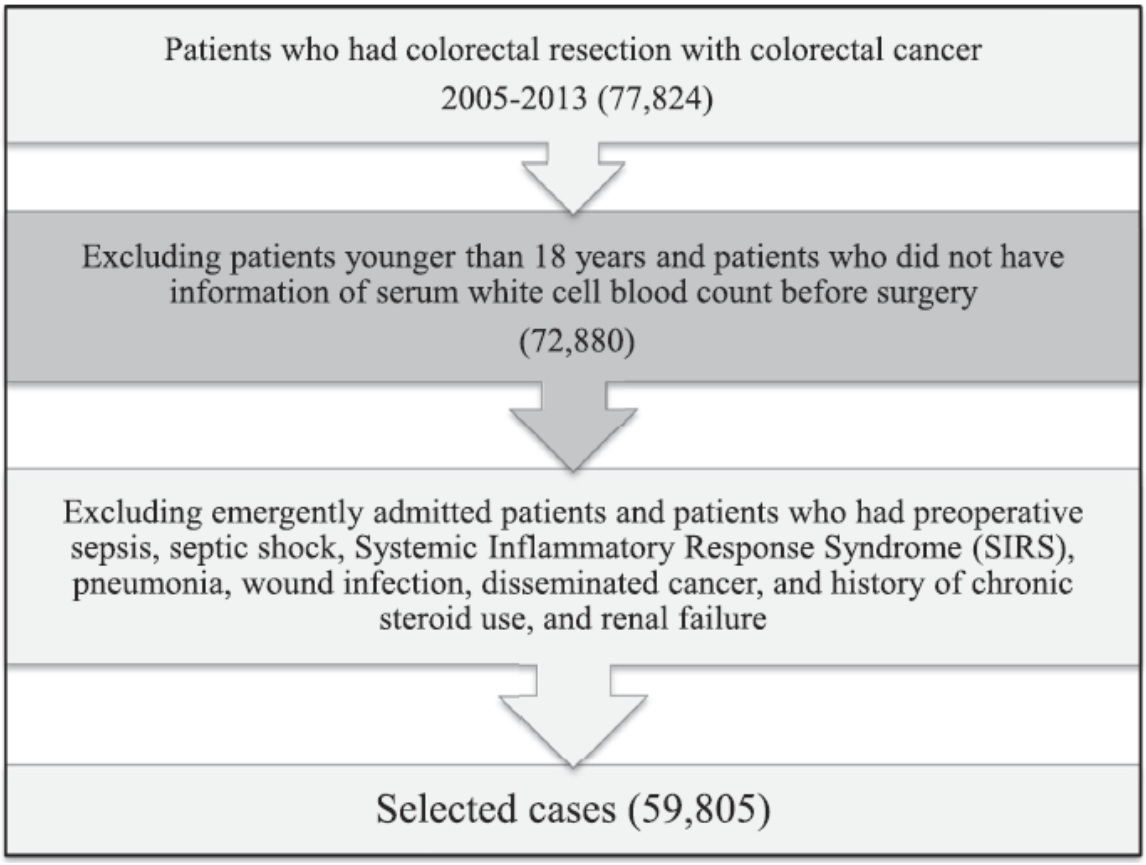

Figure 1. Inclusion and exclusion criteria in case selection for the study.

Methods

Subjects were selected from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database from 2005 to 2013.[11] The ACS NSQIP is a large, validated outcomes-based program that provides preoperative to 30-day postoperative surgical outcomes based on discharge data to improve the quality of surgical care in the United States.[11] This study evaluated patients who underwent elective colorectal resections with the diagnosis of colorectal cancer using the appropriate codes, as specified by the International Classification of Diseases, 9th Revision, clinical modifications (ICD-9-CM) diagnosis codes and Current Procedural Terminology (CPT) procedural codes. Patients who had colorectal procedures were defined based on CPT codes: 44140 to 44160, 44204 to 44212, 45110 to 45114, 45119, 45123, 45126, 45395, and 45397. Patients who underwent colorectal surgery without colorectal resection, patients admitted emergently, patients with missing data regarding preoperative serum white blood cell count (WBC), patients younger than 18 years, and patients who had preoperative sepsis, septic shock, systemic inflammatory response syndrome (SIRS), wound infection, disseminated cancer, renal failure, recent steroid use, or pneumonia within 48 hours before surgery were excluded from this study (Fig. 1). Patient diagnosis was defined based on the following ICD-9 codes: malignant neoplasm of colon and rectum (153.0 to 153.9, 154.0, 154.1, 230.3, and 230.4). Preoperative leukocytosis was defined as a blood WBC count more than 11,000/mL, in line with that reported in the literature.[12,13] Also, hypoalbuminemia was defined as a preoperative serum albumin level lower than 3.5 g/dL.

Preoperative factors analyzed included demographic factors (age, sex, and race) and 9 comorbidity conditions including history of congestive heart failure, history of dyspnea within 30 days before surgery, bleeding disorder, diabetes mellitus with use of oral agents or insulin, smoking, weight loss (more than 10% in last 6 months), history of severe COPD, ascites within 30 days before surgery, and hypertension requiring medication. Operative factors analyzed included surgical approach (open vs laparoscopic), type of procedure (partial colectomy, total colectomy, anterior resection, Hartman procedure, proctectomy, or pelvic exenteration), and wound classification (clean, clean/contaminated, contaminated, and dirty/infected). Outcomes investigated included mortality, overall morbidity, superficial surgical site infection (SSI), deep incisional SSI, organ space SSI, wound disruption, deep vein thrombosis, pneumonia, unplanned intubation, ventilator dependency more than 48 hours, pulmonary embolism, cardiac arrest requiring CPR, progressive renal insufficiency, myocardial infarction, hemorrhagic complications, acute renal failure, and prolonged hospitalization (longer than 30 days). Other factors analyzed include: preoperative serum albumin level, hematocrit, serum blood urea nitrogen/serum creatinine ratio (BUN/Cr), American Society of Anesthesiologists (ASA) score, operation length, preoperative WBC count, preoperative chemotherapy, preoperative radiotherapy, and functional health status before surgery. The overall rates of each complication were examined. Risk adjusted analysis was performed to compare the outcomes of patients with and without asymptomatic leukocytosis.

Statistical analysis

Data were analyzed using SPSS software, Version 22 (SPSS Inc.). Logistic regression analysis was used to estimate the association between preoperative leukocytosis and each outcome, including in-hospital mortality and all of the considered postoperative complications. All variables were entered into a logistic regression model. Values of $p < 0.05$ were considered statistically significant. For each outcome, the adjusted odds ratio (AOR) with 95% confidence interval was calculated and reported to estimate the relative risk associated with leukocytosis. Adjustments were made for all variables of the study.

Results

A total of 59,805 patients with the diagnosis of colorectal cancer, who underwent elective colorectal resection between 2005 and 2013, were identified. Median patient age was 66 years; the majority of the patients were white (83.5%) and male (52.5%). The most common comorbidities included hypertension (54.6%) and diabetes (18.3%). Demographic data of patients are reported in Table 1.

Among patients who underwent colorectal resection, 3,322 (5.6%) had asymptomatic leukocytosis. Mortality rates for patients with or without asymptomatic leukocytosis were 3.2% and 1.2%, respectively. In multivariate analysis of data, patients who had asymptomatic leukocytosis had significantly higher mortality (adjusted odds ratio [AOR] 1.76, $p < 0.01$) and morbidity (AOR 1.26, $p < 0.01$) (Table 2).

The risk-adjusted analysis for postsurgical complications associated with asymptomatic leukocytosis is reported in Table 2. Complications such as cardiac arrest (AOR 1.78, $p = 0.03$), unplanned intubation (AOR 1.61, $p < 0.01$), and deep incisional SSI (AOR 1.55, $p = 0.01$) were significantly higher in patients who had asymptomatic leukocytosis.

The risk-adjusted analysis for preoperative factors associated with asymptomatic leukocytosis is reported in Table 3. Factors such as serum albumin level (AOR 0.58, $p < 0.01$), BUN/Cr ratio (AOR 1.01, $p < 0.01$), smoking (AOR 1.96, $p < 0.01$), weight loss (AOR 1.78, $p < 0.01$) had associations with asymptomatic leukocytosis.

Postoperative morbidity and mortality of patients according to preoperative WBC count are illustrated in Figure 2. The highest morbidity (44%) and mortality (8%) rates occurred with WBC counts higher than 17,000/μL.

Discussion

Asymptomatic leukocytosis is a negative prognostic indicator associated with significant increase in mortality and morbidity of patients undergoing colorectal cancer surgery. Our study results show a 75% increase in mortality in patients with asymptomatic leukocytosis. Asymptomatic leukocytosis also increases the risk of 7 postoperative complications. Surprisingly, noninfectious complications of cardiac arrest, unplanned intubation, and ventilator dependency had significant associations with asymptomatic leukocytosis. We confirm previous reports indicating that asymptomatic leukocytosis is linked with poor prognosis by Kasuga and colleagues,[9] Connolly and associates,[14] and Trujillo-Santosin and coworkers.[15]

The associations between preoperative asymptomatic leukocytosis and serum albumin level in patients with asymptomatic leukocytosis may be related to the inflammatory response in such patients rather than to malnutrition. Our study results show an inverse association between serum albumin level and leukocytosis (AOR 0.58, $p < 0.01$). Serum albumin level has been introduced as a marker of malnutrition in the literature.[16,17] This correlation is in line with the previous report of an association between leukocytosis and malnutrition in cancer patients by Connolly and colleagues.[14] However, many other factors also affect the serum albumin level, such as physiologic stress. More importantly, serum albumin has been shown to be an acute phase response reactant.[18,19] A decrease in serum albumin level does not necessarily correlate directly with malnutrition, and also, an increase in serum albumin level can be the result of improvement in the overall clinical status of patients and is not necessarily due to an improved nutritional status.[18,19] Therefore, it is difficult to conclude if the association between serum albumin and asymptomatic leukocytosis is related to malnutrition or simply is related to the inflammatory response in patients with asymptomatic leukocytosis. Further clinical trial studies are indicated to evaluate the association between asymptomatic leukocytosis and serum albumin level and determine if correcting the serum albumin level can improve outcomes of patients with asymptomatic leukocytosis.

Preoperative asymptomatic leukocytosis may link with advanced colorectal cancer. Our study results show asymptomatic leukocytosis is significantly higher in patients with preoperative unintentional weight loss and patients with low serum albumin level. Preoperative weight loss and malnutrition have been previously reported as risk factors of advanced malignancy.[14,20-22] The association of leukocytosis with serum albumin level and weight loss in this study may suggest that leukocytosis identifies patients with a more aggressive disease. However, considering the limited published data on this topic, further clinical trial studies are indicated to evaluate associations between asymptomatic leukocytosis and advanced colorectal cancer.

The risks of postoperative infectious complications significantly increase in the presence of asymptomatic preoperative leukocytosis. We found significant associations between infectious complications of intra-abdominal infections, pneumonia, and deep incisional SSI with preoperative asymptomatic leukocytosis. Whether these correlations are due to the suppression of the immune system in advanced malignancy or are representing the impact of CSFs or other biomarkers, which suppress the immune system in advanced malignancy, is not clear.[9,10]

Table 1. Perioperative and Demographic Factors of Patients with Colorectal Cancer Who Have Undergone Elective Colorectal Resection

Variables	Patients without leukocytosis* (n = 56,483)	Patients with leukocytosis* (n = 3,322)	p Value
Age, y			
Mean ± SD	66 ± 13	67 ± 13	—
Median	66	68	<0.01
Sex, male, n (%)	29,626 (52.5)	1,609 (48.5)	<0.01
Race, n (%)			
White	42,398 (83.3)	2,618 (86.1)	<0.01
Black or African American	5,532 (10.9)	293 (9.6)	<0.01
Asian	2,410 (4.7)	90 (3)	<0.01
Others	563 (1.1)	39 (1.3)	0.36
Comorbidity, n (%)			
Hypertension	30,699 (54.4)	1,954 (58.8)	<0.01
Diabetes mellitus	10,214 (18.1)	712 (21.4)	<0.01
Smoking	8,059 (14.3)	844 (25.4)	<0.01
Dyspnea	5,762 (10.2)	511 (15.4)	<0.01
COPD	2,745 (4.9)	323 (9.7)	<0.01
Weight loss	2,728 (4.8)	306 (9.2)	<0.01
Bleeding disorder	1,939 (3.4)	130 (3.9)	0.14
Congestive heart failure	471 (0.8)	49 (1.5)	<0.01
Ascites	279 (0.5)	29 (0.9)	<0.01
Procedure factors			
Partial colectomy, n (%)	32,447 (57.4)	2,272 (68.4)	<0.01
Anterior resection, n (%)	13,997 (24.8)	529 (15.9)	<0.01
Proctectomy, n (%)	7,134 (12.6)	250 (7.5)	<0.01
Total colectomy, n (%)	1,734 (3.1)	119 (3.6)	<0.01
Hartman procedure, n (%)	1,011 (1.8)	137 (4.1)	<0.01
Pelvic exenteration, n (%)	160 (0.3)	15 (0.5)	0.02
Mean operation length, min ± SD	182 ± 100	173 ± 98	<0.01
Surgical approach, n (%)			
Laparoscopic	25,011 (44.3)	1,193 (35.9)	<0.01
Open	31,472 (55.7)	2,129 (64.1)	<0.01
Other factors			
Mean serum albumin level, g/dL ± SD	3.8 ± 0.5	3.5 ± 0.7	<0.01
Mean BUN/Cr ratio ± SD[§]	16 ± 6.7	16.5 ± 8.4	<0.01
Mean hematocrit, % ± SD	37.3 ± 5.4	36 ± 6	<0.01
ASA score > 2, n (%)[†]	30,042 (53.2)	2,117 (63.8)	<0.01
Dependency before surgery, n (%)[‡]	1,746 (3.1)	211 (6.4)	<0.01
Radiotherapy, n (%)	3,806 (11.4)	59 (3)	<0.01
Chemotherapy, n (%)	1,396 (4.2)	29 (1.5)	<0.01

*White blood cell count > 11,000/μL.
[†]American Society of Anesthesiologists score > 2.
[‡]Partial or complete dependency before surgery.
[§]Serum blood urea nitrogen/creatinine ratio.
ASA, American Society of Anesthesiologists; BUN/Cr, blood urea nitrogen/creatinine ratio.

Table 2. Risk-Adjusted Analysis of Outcomes Associated with Preoperative Asymptomatic Leukocytosis in Colorectal Cancer Patients Who Underwent Colon and Rectal Resection

	Patients without leukocytosis* (n = 56,483)		Patients with leukocytosis* (n = 3,322)				
Complication	**n**	**%**	**n**	**%**	**Adjusted odds ratio**	**95% CI**	**p Value**
Mortality	691	1.2	106	3.2	1.76	1.27–2.40	<0.01
Overall morbidity†	13,700	24.3	1065	32.1	1.26	1.11–1.43	<0.01
Infectious complications‡	9,148	16.2	674	20.3	1.18	1.03–1.35	0.01
Cardiac arrest	263	0.5	25	0.8	1.78	1.03–3.06	0.03
Unplanned intubation	996	1.8	121	3.6	1.61	1.22–2.13	<0.01
Deep incisional SSI	723	1.3	69	2.1	1.55	1.07–2.24	0.01
Pneumonia	1,103	2.0	127	3.8	1.46	1.10–1.94	<0.01
Ventilator dependency	846	1.5	97	2.9	1.45	1.07–1.96	0.01
Organ space SSI	1,989	3.5	149	4.5	1.43	1.10–1.86	<0.01
Deep vein thrombosis	651	1.2	57	1.7	1.13	0.74–1.73	0.54
Wound disruption	664	1.2	52	1.6	1.10	0.71–1.68	0.65
Septic shock	772	1.4	78	2.3	1.22	0.86–1.73	0.25
Hospitalization > 30 d	757	1.3	78	2.3	1.05	0.74–1.51	0.75
Hemorrhagic complications	4,019	7.1	353	10.6	1.18	0.95–1.48	0.12
Progressive renal insufficiency	465	0.8	35	1.1	1.55	0.99–2.43	0.05
Sepsis	1,797	3.2	143	4.3	1.12	0.86–1.45	0.38
Cerebrovascular complications	163	0.3	16	0.5	1.76	0.91–3.41	0.09
Urinary tract infection	1,906	3.4	119	3.6	1.08	0.83–1.42	0.53
Superficial SSI	4,032	7.1	243	7.3	0.86	0.70–1.06	0.18
Acute renal failure	302	0.5	25	0.8	0.97	0.50–1.87	0.92
Pulmonary embolism	397	0.7	28	0.8	1.17	0.66–2.04	0.58
Myocardial infarction	363	0.6	22	0.7	0.92	0.49–1.72	0.80

*White blood cell count > 11,000/μL.
†Myocardial infarction, pneumonia, ventilator dependency, unplanned intubation, cardiac arrest, acute renal failure, wound disruption, deep vein thrombosis, hemorrhagic complications, organ space SSI, superficial SSI, septic shock, urinary tract infection, deep incisional SSI, pulmonary embolism, sepsis, progressive renal insufficiency, and prolonged hospitalization.
‡Pneumonia, sepsis, septic shock, superficial SSI, organ space SSI, urinary tract infection, and deep incisional SSI.
SSI, surgical site infection

Table 3. Risk Adjusted Analysis of Preoperative Factors Associated with Asymptomatic Leukocytosis

Factors	**Adjusted odds ratio**	**95% CI**	**p Value**
Sex			
Female	Reference	Reference	Reference
Male	0.91	0.81–1.02	0.12
Age	0.99	0.98–0.99	<0.01
Comorbidity			
Smoking	1.96	1.71–2.24	<0.01
COPD	1.34	1.09–1.64	<0.01
Weight loss	1.78	1.49–2.14	<0.01
Diabetes mellitus	1.04	0.90–1.21	0.51
Hypertension	1.09	0.96–1.24	0.15
Dyspnea	1.14	0.97–1.34	0.08
Congestive heart failure	0.99	0.63–1.56	0.98
Bleeding disorder	0.95	0.72–1.24	0.71
Ascites	0.67	0.37–1.19	0.17
Other factors			
American Society of Anesthesiologists Score > 2	1.21	1.07–1.38	<0.01
Serum albumin level	0.58	0.52–0.64	<0.01
BUN/Cr ratio*	1.01	1.007–1.24	<0.01
Hematocrit	0.99	0.98–1	0.64
Dependency before surgery†	1.20	0.97–1.50	0.08
Chemotherapy	0.73	0.46–1.15	0.17
Radiotherapy	0.21	0.15–1.30	0.10

*Serum blood urea nitrogen/creatinine ratio.
†Partial or complete dependency before surgery.

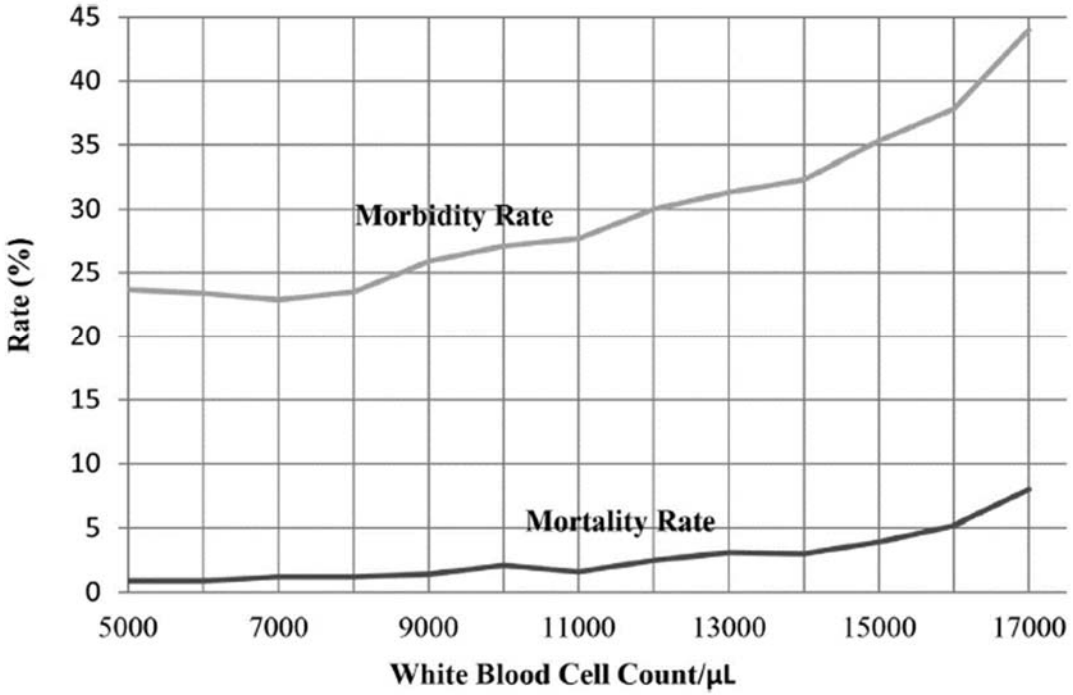

Figure 2. Mortality and morbidity of colorectal cancer patients who underwent colorectal resection by white blood cell count.

Preoperative dehydration may play a role in the pathogenesis of asymptomatic leukocytosis. Our results show preoperative asymptomatic leukocytosis has a strong association with preoperative serum BUN/Cr ratio. We found that with increasing BUN/Cr ratio the risk of leukocytosis increases. The BUN/Cr ratio has been previously identified as a marker of dehydration.[23-26] Also, associations between dehydration and acute phase reactants have been reported previously.[19] Considering that 27% of patients who undergo colorectal resection have preoperative dehydration, probably due to preoperative bowel preparations and time of fasting, treatment of dehydration before operation may decrease the rate of asymptomatic leukocytosis and improve outcomes of surgical patients.[26]

Our study results show significant associations between asymptomatic leukocytosis and postoperative ventilator dependency and unplanned intubation. The mechanisms responsible for the association demonstrated by this analysis are unclear. However, this can be partially explained with higher rates of malnutrition (low serum albumin levels) in patients with asymptomatic leukocytosis.[14] Preoperative malnutrition has been known as an important risk factor for postoperative ventilator dependency.[27] We also found a significant association between asymptomatic preoperative leukocytosis and postoperative intra-abdominal SSIs, including anastomotic leakage. The mechanisms responsible for the association demonstrated by this analysis are unclear. However, this may partly be explained by a higher rate of malnutrition in patients with asymptomatic leukocytosis.[14] Preoperative malnutrition has been reported as a risk factor for anastomotic leakage.[28]

Correcting the reducible predictors of asymptomatic leukocytosis may decrease mortality and morbidity of patients. Although this study introduced 7 factors that had associations with asymptomatic leukocytosis, the risk factors are nonreducible, except for serum albumin level and preoperative dehydration. Although the retrospective nature of this study makes any conclusion difficult, correcting the serum albumin level and hydration before surgery may have benefits for patients with asymptomatic leukocytosis. However, further clinical trials are indicated to evaluate if hydrotherapy and nutritional support can decrease mortality and morbidity of such patients.

Study limitations

There are several limitations to our study. This study is a retrospective review and is subject to typical biases for retrospective studies, such as selection bias. Another limitation was that data in this study were extracted from a large national database in the US, and the wide variation in hospital setting, hospital quality, surgical strategy, and surgeon expertise can confound the study. Also, coding errors in data collection may exist because of the use of discharge data in the NSQIP database.[29] Although in this study we excluded patients who had preoperative sepsis, septic shock, systemic inflammatory response syndrome, renal failure, pneumonia, and wound infection from the study, and we included only patients who had elective operations, we did not have complete information about all possible preoperative occult infections such as urinary system occult infections that can cause or contribute to leukocytosis. Another limitation was that the NSQIP database does not include some potentially important details such as neutrophil/lymphocyte ratio, tumor stage, tumor markers, and pathologic nature of tumors. Despite these limitations, this study is one of the first that has reported on the associations between asymptomatic leukocytosis and postoperative complications in colorectal resection procedures using multivariate analysis.

Conclusions

Of patients who underwent elective colorectal resection with the diagnosis of colorectal cancer, 5.6% had preoperative asymptomatic leukocytosis from 2005 to 2013. Preoperative asymptomatic leukocytosis has associations with increased mortality, morbidity, and postoperative complications in colorectal cancer surgery. The risks of postoperative ventilator dependency, unplanned intubation, and organ space SSI increase with the presence of preoperative asymptomatic leukocytosis. There is a strong association between preoperative asymptomatic leukocytosis with preoperative dehydration and serum albumin level. Further studies are indicated to validate these findings, gain a better understanding of the mechanisms involved, and improve the ability to affect these pathways.

Author Contributions

Study conception and design: Moghadamyeghaneh, Hanna, Carmichael, Mills, Pigazzi, Stamos
Acquisition of data: Moghadamyeghaneh
Analysis and interpretation of data: Moghadamyeghaneh
Drafting of manuscript: Moghadamyeghaneh, Hanna, Carmichael, Mills, Pigazzi, Stamos
Critical revision: Moghadamyeghaneh, Hanna, Carmichael, Mills, Pigazzi, Stamos

References

1. Shike M, Winawer SJ, Greenwald PH, et al. Primary prevention of colorectal cancer. The WHO Collaborating Centre for the Prevention of Colorectal Cancer. Bull World Health Organ 1990;68:377e385.
2. American Cancer Society.Cancer Facts and Figures 2014. Atlanta, Ga: American Cancer Society. Available at: http://www.cancer.org/research/cancerfactsstatistics/cancerfactsfigures2014/index; 2014. Accessed April 8, 2015.
3. Newton KF, Newman W, Hill J. Review of biomarkers in colorectal cancer. Colorectal Dis 2012;14:3e17.
3. Yang X, Liu F, Xu Z, et al. Expression of granulocyte colony stimulating factor receptor in human colorectal cancer. Postgrad Med J 2005;81:333e337.
4. Asano S, Urabe A, Okabe T, et al. Demonstration of granulopoietic factor(s) in the plasma of nude mice transplanted with a human lung cancer and in the tumor tissue. Blood 1977;49: 845e852.
5. Avalos BR, Gasson JC, Hedvat C, et al. Human granulocyte colony-stimulating factor: biologic activities and receptor characterization on hematopoietic cells and small cell lung cancer cell lines. Blood 1990;75:851e857.
6. Ninci EB, Brandstetter T, Meinhold-Heerlein I, et al. G-CSF receptor expression in ovarian cancer. Int J Gynecol Cancer 2000;10:19e26.
7. Tachibana M,Miyakawa A, Uchida A, et al. Granulocyte colonystimulating factor receptor expression on human transitional cell carcinoma of the bladder. Br J Cancer 1997;75:1489e1496.
8. Kasuga I, Makino S, Kiyokawa H, et al. Tumor-related leukocytosis is linked with poor prognosis in patients with lung carcinoma. Cancer 2001;92:2399e2405.
9. Tibaldi C, Vasile E, Bernardini I, et al. Baseline elevated leukocyte count in peripheral blood is associated with poor survival in patients with advanced non-small cell lung cancer: a prognostic model. J Cancer Res Clin Oncol 2008;134:1143e1149.
10. National Surgical Quality Improvement Program. Chicago, IL: American College of Surgeons. Available at: www.acsnsqip.org; 2005. Accessed January 17, 2012.
11. Khuri SF, Daley J, Henderson W, et al. The Department of Veterans Affairs' NSQIP: the first national, validated, outcome-based, risk-adjusted, and peer-controlled program for the measurement and enhancement of the quality of surgical care. National VA Surgical Quality Improvement Program. Ann Surg 1998;228:491e507.
12. Mahid SS, Polk HC, Lewis JN, Turina M. Opportunities for improved performance in

surgical specialty practice. Ann Surg 2008;247:380e388.
13. Connolly GC, Khorana AA, Kuderer NM, et al. Leukocytosis, thrombosis and early mortality in cancer patients initiating chemotherapy. Thromb Res 2010;126:113e118.
14. Trujillo-Santos J, Di Micco P, Iannuzzo M, et al. Elevated white blood cell count and outcome in cancer patients with venous thromboembolism. Findings from the RIETE Registry. Thromb Haemost 2008;100:905e911.
15. Gariballa SE. Malnutrition in hospitalized elderly patients: when does it matter? Clin Nutr 2001;20:487e491.
16. Church JM, Hill GL. Assessing the efficacy of intravenous nutrition in general surgical patients: dynamic nutritional assessment with plasma proteins. JPEN J Parenter Enteral Nutr 1987;11:135e139.
17. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. N Engl J Med 1999;340:448e454.
18. Banh L. Serum proteins as markers of nutrition: what are we treating? Pract Gastroenterol 2006;30:46e64.
19. Monreal M, Fernandez-Llamazares J, Pinõl M, et al. Platelet count and survival in patients with colorectal cancerea preliminary study. Thromb Haemost 1998;79: 916e918.
20. Wie GA, Cho YA, Kim SY, et al. Prevalence and risk factors of malnutrition among cancer patients according to tumor location and stage in the National Cancer Center in Korea. Nutrition 2010;26:263e268.
21. Kiran PR, Glass RE. Duration of symptoms and spread of colorectal cancer: a short history does not mean early disease. Ann R Coll Surg Engl 2002;84:381e385.
22. Jurado R, Mattix H. The decreased serum urea nitrogencreatinine ratio. Arch Intern Med 1998;158:2509e2511.
23. Sklar AH, Riesenberg LA, Ur Rehman A, et al. Prerenal azotemia: differentiation of hyperureagenesis from renal hypoperfusion using urinary urea nitrogen data. Int J Artif Organs 1996;19:164e169.
24. Feinfeld DA, Bargouthi H, Niaz Q, Carvounis CP. Massive and disproportionate elevation of blood urea nitrogen in acute azotemia. Int Urol Nephrol 2002;34:143e145.
25. Moghadamyeghaneh Z, Phelan MJ, Carmichael JC, et al. Preoperative dehydration increases risk of postoperative acute renal failure in colon and rectal surgery. J Gastrointest Surg 2014;18:2178e2185.
26. Arozullah AM, Daley J, Henderson WG, Khuri SF. Multifactorial risk index for predicting postoperative respiratory failure in men after major noncardiac surgery. The National Veterans Administration Surgical Quality Improvement Program. Ann Surg 2000;232:242e253.
27. Kang CY, Halabi WJ, Chaudhry OO, et al. Risk factors for anastomotic leakage after anterior resection for rectal cancer. JAMA Surg 2013;148:65e71.
28. Lorence DP, Ibrahim IA. Benchmarking variation in coding accuracy across the United States. J Health Care Finance 2003;29:29e42.

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