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Season and vitamin D status do not affect probability for surgical site infection after colorectal surgery

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Summary

Background Regardless of reports on the prevalence of hypovitaminosis D and seasonal effects in the general population and significant worsening of many outcomes there is a scarcity of studies focusing on surgical patients. We, therefore, designed a study to assess the association and difference in surgical-wound infections between patients having colorectal surgery in winter compared with patients having surgery in summer months.

Methods Patients were divided into winter and summer surgical procedures depending on their date of surgery. The relationship between seasons (and Vitamin D) and primary outcome of wound infections using multivariable logistic regression was assessed.

Results Out of 2919 patients, 241 (7.7 %) experience surgical site infection. The observed incidence of any surgical site infection postoperatively was 6.8 %, 9.9 %, 7.3 %, and 8.2 % for patients having surgery in spring, summer, fall, and winter, respectively. Furthermore, vitamin D concentration was not associated with incidence of surgical site infection (Odds Ratio (OR): 0.51(0.01, 27) for a one-unit increase in vitamin D concentration; $p = 0.74$).

Conclusion Our analysis suggests that perioperative vitamin D concentration is not associated with surgical site infections in colorectal surgical patients, likely because the outcomes are overwhelmingly determined by other baseline and surgical factors.

Keywords Seasons · Vitamin D · Surgical-wound infection · Colorectal surgery

Introduction

Colorectal surgery is associated with a high rate of surgical site infection (SSI). SSIs occur in about 11–28 % of all patients who undergo colorectal surgery [1, 2]. There is increasing awareness of the need to reduce SSI given that development of this complication adversely affects length of hospitalization, quality of life, other major postoperative outcomes, and increase cost [3, 4]. Further-

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more, infections are increasingly been used as a quality of care measure by government and private agencies to improve surgical care and reduce infections [1].

Multiple factors play role in surgical infections, some of this can be modified and outcomes improved. Immune system of the patient plays a crucial role in prevention and controlling of infections. Infections such as cold, flu, and chest infections are generally more common in the winter. It is suggested that the upsurge in infections seen in the winter may be associated with lower concentration of vitamin D. Vitamin D (25-hydroxyvitamin D) insufficiency (25–75 nmol/L or 10–30 ng/mL) or deficiency (< 25 nmol/L or < 10 ng/mL) affects > 1 billion people worldwide [5], spanning age groups, gender, and ethnicities [3]. Vitamin D plays an important part in the immune system and patients with Vitamin D deficiency have substantially higher percentages of risk for cancer and infections [6, 7]. 1, 25 (OH) 2D acts as an immune system modulator, preventing excessive expression of inflammatory cytokines and increasing the "oxidative burst" potential of macrophages. Perhaps, most importantly, it dramatically stimulates the expression of potent antimicrobial peptides, which exist in neutrophils, monocytes, natural killer cells, and in epithelial cells, where they play a major role in protecting the body from infections.

There are few studies evaluating the influence of season on patient. Kocer et al. [8] evaluated prognostic factors for morbidity and mortality in patients undergoing surgical procedure for peptic ulcer perforations. They confirmed that winter season is an independent worse predictor of morbidity and mortality. Shuhaiber et al. [9] showed that in winter hospital mortality and intensive care unit length of stay increased compared with other seasons in patients undergoing cardiac surgery. Recently, Turna et al. [10] showed a significant effect of season on survival following surgical resections for non-small-cell lung carcinoma. Despite reports on the prevalence of hypovitaminosis D and seasonal effects in the general population and significant worsening of many outcomes with vitamin D deficiency there is a scarcity of studies focusing on surgical patients. There is no study in literature to recognize the association between seasons and wound infection after colorectal surgery.

We thus tested the primary hypothesis that surgical-wound infections in patients having colorectal surgery in winter will be increased compared with patients having surgery in summer months. Secondarily, we tested the hypothesis that patients with low vitamin D concentration will have higher postoperative infections after colorectal surgery.

Methods and materials

With Cleveland Clinic Foundation IRB approval, this retrospective cohort analysis was based on patients who had colorectal surgery at the Cleveland Clinic. Perioperative and the outcome variables were obtained from the Cleveland Clinic Perioperative Health Documentation System database. Patients were divided into winter and summer surgical procedures depending on their date of surgery. January, February, and March months were accepted as winter. June, July, and August were accepted as summer months. All patients who had any measured vitamin D were considered for secondary analysis in this study. Vitamin D levels were obtained from Cleveland Clinic Perioperative Health Documentation System database, starting 3 months prior procedure date to 1 month after for all available patients in the colorectal surgery wound infection registry. Vitamin-D sufficiency was defined as a serum 25(OH) D level of 32 ng/mL. Vitamin-D inadequacy was defined as a serum 25(OH) D level of < 32 ng/mL and was further divided into vitamin-D insufficiency (20 to < 32 ng/mL) and vitamin-D deficiency (< 20 ng/mL) [3]. Pediatric patients and patients with missing covariable information were excluded from the study.

The relationship between seasons (and Vitamin D) and primary outcome of wound infections using multivariable logistic regression was assessed. The sources of confounding factors were removed by adjusting for all baseline variables (including but not limited to demographics, diagnoses, type of procedure) as well as intraoperative variables (including but not limited to intraoperative blood transfusions and length of surgery). The analyses included descriptive and statistical assessments of the shape of the relationship between seasons and outcome (i.e., whether it is linear, quadratic, etc).

For the *primary analysis*, the relationship between seasons (spring: March 21–June 20; summer: June 21–September 22; fall: September. 23–December 20; and winter: December 21–March 20) and SSI was assessed using multivariable logistic regression. Pair wise comparisons among the seasons (for a total of six comparisons) were performed, among which comparison between winter and summer was prespecified as the primary comparison. The significance criterion was 0.025 for the primary comparison, and was 0.005 (i.e., 0.025/5) for the other five comparisons to control the overall type I error at 5 % for all six comparisons. The following prespecified covariables were adjusted for in the analysis: age, gender, race, body mass index, American Society of Anesthesiologist (ASA) physical status, preoperative usage of steroids, diabetes, chronic renal failure, emergent case, duration of surgery, and amount of red blood cell transfusion.

The *secondary analysis* was the relationship between Vitamin D concentration and infections was assessed using multivariable logistic regression. All patients who had any measured vitamin D were included for secondary analysis in this study.

A total of 1638 patients who underwent colorectal surgery in winter (708) or summer (930), and observed incidence of 10 % of patients having surgery in summer experienced infection, we had about 90 % power to detect an odds ratio of 0.54 or less at the 0.05 significance level. SAS software version 9.3 (SAS Institute, Cary, NC, USA) was used for all analyses.

Results

In all, 2985 patients underwent colorectal surgery at the Cleveland Clinic Main Campus between June 2010 and March 2012. Exclusions were patients younger than 18, with ASA physical status > 4, or with missing covariables, yielding a total of 2919 patients for our analysis. Table 1 shows the summary statistics of baseline and intraoperative characteristics by seasons.

Out of 2919 patients, 241 (7.7 %) experience SSI, including 125, 11, and 126 organ, deep, and superficial SSIs, respectively. The observed incidence of any SSI postoperatively was 6.8, 9.9, 7.3, and 8.2 % for patients having surgery in spring, summer, fall, and winter, respectively. For informational purposes, the observed incidence of SSI by month of surgery is provided in Fig. 1.

There was no significant overall seasonal effect on postoperative infection, after adjusting for covariables ($p = 0.08$). Furthermore, no significant difference was found between any two seasons (Table 2). The estimated odds ratio was 1.28 (97.5 % confidence interval (CI): 0.86, 1.92) for having surgery in summer as compared with winter ($p = 0.16$). The biggest difference in infection was between summer (9.9 %) and spring (6.8 %) (OR (99.5 % CI): 1.64(0.86, 3.15); $p = 0.03$).

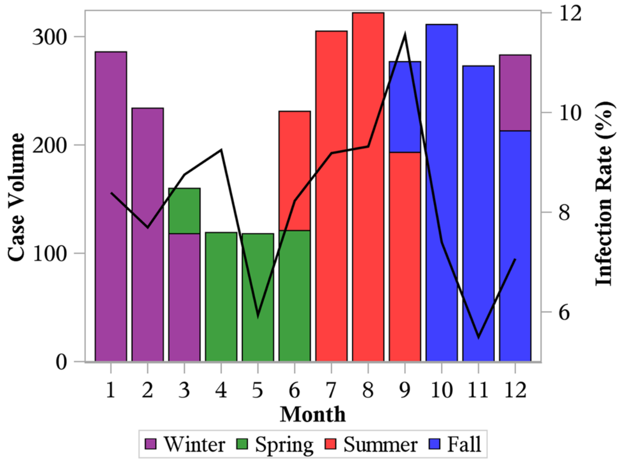

Fig. 1 Number of colorectal surgeries and incidence of surgical site infection (including organ, deep, and superficial surgical site infections) by month. (N = 2,919)

In a post-hoc analysis, no significant difference was found on the incidence of any SSI between rectal surgery (6.7 %, 45/670) and colon surgery (8.7 %, 196/2250) ($p = 0.10$).

Table 1 Demographics preoperative and intraoperative characteristics by seasons[a] ($n = 2919$)

Variable	Spring ($n = 400$)	Summer ($n = 930$)	Fall ($n = 881$)	Winter ($n = 708$)	*p*-Value[b]
Age, years	53 ± 17	52 ± 17	53 ± 17	52 ± 16	0.55[c]
Gender (female), *n* (%)	190 (48)	465 (50)	446 (51)	391 (55)	0.06
Race, *n* (%)					0.77
White	357 (89)	853 (92)	799 (91)	638 (90)	
Black	31 (8)	53 (6)	59 (7)	53 (7)	
Others	12 (3)	24 (3)	23 (3)	17 (2)	
BMI (kg/m^2)	27 ± 6	27 ± 6	27 ± 7	27 ± 6	0.99[c]
ASA status, *n* (%)					0.47
1	13 (3)	28 (3)	30 (3)	21 (3)	
2	172 (43)	478 (51)	438 (50)	348 (49)	
3	197 (49)	392 (42)	381 (43)	314 (44)	
4	18 (5)	32 (3)	32 (4)	25 (4)	
Diabetes, *n* (%)	70 (18)	180 (19)	181 (21)	148 (21)	0.51
Chronic renal failure *n* (%)	26 (7)	36 (4)	42 (5)	30 (4)	0.20
Usage of steroids, *n* (%)	31 (8)	81 (9)	74 (8)	70 (10)	0.62
Emergency, *n* (%)	29 (7)	33 (4)	37 (4)	30 (4)	0.02
Type of surgery, *n* (%)					0.85
Rectal	94 (24)	208 (22)	210 (24)	158 (22)	
Colon	306 (77)	722 (78)	672 (76)	550 (78)	
Duration of surgery (hours)	4 [2, 5]	3 [2, 5]	3 [2, 5]	3 [2, 5]	0.06[d]
RBC transfusion (ml)	0 [0, 0]	0 [0, 0]	0 [0, 0]	0 [0, 0]	0.13[d]

Summary statistics are presented as number (%) of patients, mean ± SD, or median [Q1, Q3]
ASA American Society of Anesthesiologist, *BMI* body mass index, *RBC* red blood cell
[a]Spring: March 21–June 20; summer: June 21–September 22; fall: September 23–December 20; and winter: December 21–March 20
[b]Pearson's Chi-Squared Test, unless specified
[c]Analysis of variance
[d]Kruskal–Wallis test

Table 2 Primary results—association between seasons[a] and surgical site infection for colorectal surgical patients ($n=2919$)

Comparison	Odds ratio (CI)[b]	p^b
Spring versus summer	0.61 (0.32, 1.17)	0.03
Spring versus fall	0.86 (0.44, 1.70)	0.54
Spring versus winter	0.78 (0.39, 1.56)	0.31
Summer versus fall	1.42 (0.87, 2.30)	0.04
Summer versus winter, primary comparison	*1.28 (0.78, 2.12)*	*0.16*
Fall versus winter	0.91 (0.53, 1.55)	0.60

[a]Spring: March 21–June 20; summer: June 21–September 22; fall: September 23–December 20; and winter: December 21–March 20
[b]The significance criterion was 0.025 for the primary comparison, and was 0.005 (i.e., 0.025/5) for the other five comparisons to control the overall type I error at 5 % for all six comparisons

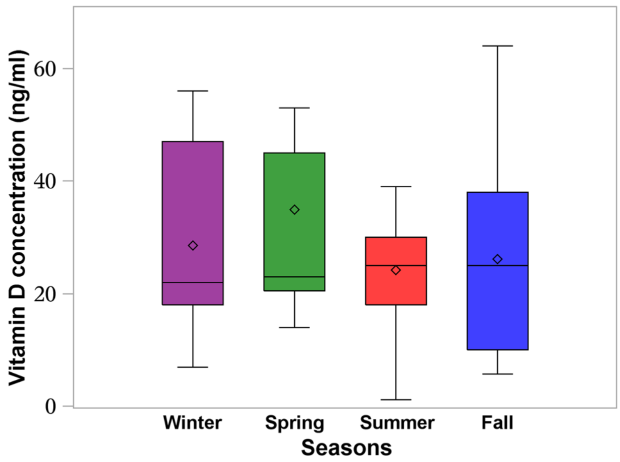

Fig. 2 Season dependent vitamine D concetrations. Values were assessed, as described in Methods.

Out of 2919 patients, only 62 had a 25-hydroxyvitamin D measurement between 3 months before surgery and 1 month after the surgery. The median [Q1, Q3] difference between the date of 25-hydroxyvitamin D measurement and the date of surgery was 11 [–8, 50] days (i.e., 11 days before surgery). The observed median vitamin D concentration was 24.5 [Q1, Q3: 18, 34] ng/ml, which was descriptively similar across the seasons (Fig. 2, Appendix). Furthermore, vitamin D concentration was not associated with incidence of SSI (OR: 0.51(0.01, 27) for a one-unit increase in vitamin D concentration; $p=0.74$).

Discussion

Postoperative SSIs are the most common complications after colorectal surgery. Incidence is variable and ranges from 10 to 40 %. Our results demonstrated almost 8 % infections in this high-risk patient population, although on the low side of the range it is still significant. Considering the cost of prolonged stay and treatments associated with SSIs, which puts significant burden on the health system and patients.

We found no significant difference between seasons and incidence of SSI after colorectal surgery. Although not significant there was a trend towards lower infection rates in spring (30 %) when compared with summer. This result is surprising and contrary to our hypothesis. There is no available study to compare in the literature evaluating seasonality of surgical infections after colorectal surgery. However, there are few studies in other surgical population supporting our results. LaPar et al. [11] reported that, the morbidity and mortality of patients were lowest in patients operated in spring after lung resection and Kestle et al. [12] reported that complications such as infection and wound dehiscence were higher in July and August after pediatric shunt surgery. Gruskay et al. [13] very similar to our results found that surgical infections decreased to the lowest point in the spring (2.8 %) when compared with summer (4.1 %), although the overall infection rates were lower because of type of surgery.

Clinical importance of understanding seasonality of colorectal surgical infections is important, although some may argue that this may not be a modifiable factor. We believe that by understanding the mechanisms behind seasonality of colorectal surgical infections will help us in developing prevention strategies. There are multiple possible mechanisms suggested; Loffeld et al. [14] suggested that increased infections during the summer was result of thinner and looser clothing in hospitals resulting in more contact. Increased contact was suggested to be a determinant cause for the increased rates of infection. Supporting this, high temperature and humidity has been shown to promote bacterial growth in the skin, which either directly from patient or from hospital staff could contaminate the surgical site. Bacteria responsible for surgical infection also changes in the warm and humid weather. Hospitals are usually well-cooled in summer but still we cannot exclude this as a possibility of increased infections.

Another possible explanation could be the “July” effect, which is defined as the time when new inexperienced trainees (residents and fellows) are starting to work. Although there are numbers of studies which demonstrated no such effect, few other studies have shown that inexperience affects outcomes. It is reasonable to assume that experience affects intraoperative blood loss, surgical time, and aseptic technique which are associated with SSIs. Our study was done in one single academic center, which leaves us open to “July” effect but majority of the residents do rotate in different services periodically which means that there are inexperienced trainees throughout the year.

Vitamin D has significant immune modulating and antimicrobial function, supporting these a recent study from our institution confirmed that vitamin D concentration ≤ 13 ng/mL after undergoing noncardiac surgery resulted in more infection rate (13.3 %) compared with those vitamin D concentration ≥ 32.6 ng/mL resulted in less postoperative infection rate (4.6 %) [15]. However, we found no association with vitamin D levels and SSI. This probably is related to limited number of patients in our patient population who has vitamin D measurement.

As with any all-retrospective studies, our ability to adjust for potential confounding is limited to available data. Although we accounted for potential confounding effects of patients', intraoperative and surgical factors, residual bias due to uncontrolled confounding variables may remain possible. There are some limitations in our study which must be addressed. Most importantly, we did not include all possible parameters which may affect the occurrence of infection in colorectal surgery patients.

This is the first clinical study evaluating the effect of seasons on postoperative SSIs after colorectal surgery. The basis for our analysis was compelling laboratory and epidemiologic evidence that seasons and vitamin D concentrations are critical for the resistance to infection. Although there was no statistical difference between seasons there was a trend of decreased infections in spring and a trend of increase in summer months. These results justify a large clinical trial comparing different climate zones and academic versus private institutions.

Ethical and administrative section

Potential benefits: None.
Potential risks: None.
Cost to the subjects: None.
Reimbursement of the subjects: None.
Confidentiality of records: Names of patients and other identifiable data will not be presented.

Conflict of interest

The authors declare that there are no actual or potential conflicts of interest in relation to this article.

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