Gynecologic Oncology 137 (2015) 523–528

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Post-operative enteral immunonutrition for gynecologic oncology patients undergoing laparotomy decreases wound complications☆

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HIGHLIGHTS

- Surgical site infections (SSIs) in gynecologic oncology patients undergoing laparotomy can be decreased with provision of an immune modulating diet.
- Immune modulating diets may protect against the morbidity associated with treatment for SSIs.

ARTICLE INFO

Article history:
Received 14 January 2015
Accepted 1 April 2015
Available online 16 April 2015

Keywords:
Surgical site infections
Malnutrition
Post-operative
Complications
Immune-modulating diets

ABSTRACT

Objectives. The aim of this study is to determine if peri-operative immune modulating dietary supplements decrease wound complications in gynecologic oncology patients undergoing laparotomy.

Methods. In July 2013 we instituted a practice change and recommended pre- and post-operative oral immune modulating diets (IMDs) to patients undergoing laparotomy. We retrospectively compared patients who received IMDs to those who did not for the study period July 2012 to June 2014. Our outcome of interest was the frequency of Centers for Disease Control surgical site infections (CDC SSIs).

Results. Of the 338 patients who underwent laparotomy during the study period, 112 (33%) received IMDs post-operatively. There were 89 (26%) wound complications, including 69 (78%) CDC SSI class 1, 7(8%) class 2 and 13(15%) class 3. Patients receiving IMDs had fewer wound complications than those who did not (19.6% vs. 33%, $p = 0.049$). After controlling for variables significantly associated with the development of a wound complication (ASA classification, body mass index (BMI), history of diabetes mellitus or pelvic radiation, length of surgery and blood loss) consumption of IMDs remained protective against wound complications (OR 0.45, CI 0.25–0.84, $p = 0.013$) and was associated with a 78% reduction in the incidence of CDC SSI class 2 and 3 infections (OR = 0.22, CI 0.05–0.95, $p = 0.044$).

Conclusions. Post-operative IMDs are associated with fewer wound complications in patients undergoing laparotomy for gynecologic malignancy and may reduce the incidence of CDC SSI class 2 and 3 infections.

1. Introduction

Surgical site infections (SSIs) significantly increase peri-operative morbidity and the economic costs related to surgery [1–3]. Malnutrition has long been shown in multiple surgical populations, including gynecologic oncology patients, to be an independent risk factor for the development of SSIs [4–7]. The high rates of malnutrition at the time of diagnosis make gynecologic oncology patients even more vulnerable to SSIs and the associated morbidity [8]. Malignancy related malnutrition causes alterations in immune function that impairs a patient's response to surgical stress and places malnourished surgical patients at increased risk for the development of SSIs [9,10].

Preventing or treating malnutrition to improve surgical morbidity has been the subject of decades of research [11]. Early initiation of enteral feeding in patients who have undergone abdominal surgery has been shown to decrease infectious complications and hospital length of stay [12]. To address the immune defects associated with the malnourished state, "immunonutrients"—arginine, glutamine, omega-3 fatty acids and nucleotides—have been incorporated into enteral supplements and studied in post-operative cardiac surgery patients as well as in gastrointestinal and head and neck malignancy patients [13–17]. Use of an immune modulating diet (IMD) has demonstrated significantly

☆ The authors have no financial conflicts of interest to disclose.

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http://dx.doi.org/10.1016/j.ygyno.2015.04.003
0090-8258/

decreased rates of post-operative complications in these cohorts of high-risk patients undergoing major surgery. Specifically, patients receiving peri-operative IMDs have decreased rates of post-operative infectious complications as well as shorter lengths of hospital stay as compared to patients receiving standard enteral diets. However, none of these studies have been conducted in a gynecologic oncology surgical population.

Malnutrition has been demonstrated to affect 24–67% of gynecologic cancer patients at the time of diagnosis and portends poor surgical outcomes [4,8,18]. We hypothesized that gynecologic oncology patients undergoing laparotomy would be a high risk surgical population for which an intervention to treat or prevent the malnourished state would reduce the frequency and severity of SSIs. As such, we sought to determine if providing peri-operative enteral immunonutrition for gynecologic oncology patients undergoing laparotomy was associated with decreased rates of post-operative SSIs.

2. Patients & methods

In the academic year beginning July 2013 the division of Gynecologic Oncology at the University of San Francisco California (UCSF) instituted a quality improvement measure to improve post-surgical wound infections in patients on the gynecologic oncology service undergoing laparotomy. The only commercially available supplement that contains arginine, dietary nucleotides and omega-3 fatty acids is a product called Impact (Nestle Health Science) and this product has been extensively studied in other post-operative surgical populations [13]. Impact contains 4.2 g of arginine, 430 mg of nucleotides, and 1.1 g of eicosapentanoic/docosahexanoic omega-3 fatty acids in each 247 mL serving. We instructed patients to drink three servings of Impact per day 5 days prior to and after surgery based on the results of a meta-analysis of high risk surgical patients that suggested IMDs may provide the most benefit when initiated at least 5 days prior to the surgical insult [13]. Patients were provided with information to arrange for outpatient home delivery of Impact and were directed to the hospital gift shop where the supplement was also available for purchase. Inpatient nutrition services stocked Impact for diet supplementation post-operatively. Early feeding within 24 h of surgery is standard post-operative care for our surgical patients and all patients who underwent laparotomy were given Impact orally three times daily during the post-operative hospitalization.

After obtaining approval from our Institutional Review Board, we performed a retrospective cohort study of gynecologic oncology patients undergoing open surgery at UCSF between July 1, 2012 and June 30, 2014. We identified 338 patients meeting these criteria. Although patients who had a laparoscopy converted to laparotomy did not receive pre-operative counseling regarding Impact supplementation, these patients were provided with a post-op IMD and were included in the analysis. Abstracted variables included patient demographics, primary cancer diagnosis, prior cancer treatments including chemotherapy and pelvic radiation, length of surgery, length of hospital stay, estimated blood loss (EBL), type of surgery, intra-operative complications, post-operative complications, provision of total parenteral nutrition (TPN), American Society of Anesthesiology (ASA) classification, diabetes, pre-and post-operative albumin levels, Impact consumption and tumor histology, stage, and grade. Analysis of our publically reported surgical care improvement project (SCIP) data indicates, we were 100% compliant with appropriate antibiosis type and timing in hysterectomy patients (67% of cases). Compliance for other surgical case types was assumed to be nearly as good and this data was not abstracted separately.

Our primary outcome variable was wound infection within 30 days of surgery. Wound infection was classified into three categories based on the Center for Disease Control surgical site infection (CDC SSI) criteria—superficial, deep and organ/space infections [19].

3. Statistical analysis

Univariate analysis was performed to identify predictors of SSI, using chi squared or Fisher exact tests for categorical variables and the Wilcoxon rank sum test for continuous variables. All variables with a p-value < 0.20 were incorporated into multivariable logistic regression analysis, and stepwise and backward variable selection methods were used in an iterative fashion for the final model. Variables with a p-value < 0.05 were retained. Data were analyzed using Stata version 13 and R [20,21].

4. Results

There were 338 patients who underwent open surgery during the study period; 149 patients underwent surgery following implementation of our protocol, while 189 underwent surgery during the preceding year. Of the 338, 112 (33%) received IMDs post-operatively. Compliance with the post-operative administration of Impact after protocol implementation was 75% (112/149). Of the 149 patients who were eligible for post-operative Impact after protocol implementation, there were no differences in clinical characteristics between the 37 patients who did not consume Impact and the 112 who did (see supplementary table 1). Only 5 patients took Impact preoperatively. The group of patients who received IMDs had a higher incidence of ovarian, fallopian or peritoneal cancer diagnoses and a lower incidence of benign diagnoses than patients receiving standard post-operative diets ($p < 0.05$). Other clinical characteristics and operative characteristics were not significantly different between the groups (Table 1).

In our cohort there were 89 (26%) wound infections within 30 days of surgery. Of these, 69 (78%) were classified as CDC SSI class 1, 7 (8%) as class 2, and 13 (15%) as class 3 (Fig. 1). Univariate analysis identified ASA classification greater than or equal to 2, body mass index (BMI) > 30, history of diabetes mellitus or pelvic radiation, length of surgery, surgical blood loss greater than or equal to 1 L and administration of post-operative total parenteral nutrition to be independently associated with the development of a post-operative wound infections ($p < 0.05$) (Table 2). Incision type, gynecologic cancer organ of origin, histology, stage, and grade were not significantly associated with the development of a wound infection. Patients with a post-operative diagnosis of gastrointestinal cancer were more likely to develop a SSI ($p = 0.0005$). The majority of patients (69%) received between 1 and 4 days of Impact. The duration of Impact consumption (1–4 days versus greater than or equal to 5 days) was not significantly associated with SSIs ($p = 0.116$).

Of the 145 patients for whom pre-operative albumin levels were collected, 50 patients (34%) had subnormal levels (<3.5 g/dL). Thirty-two percent of patients with hypoalbuminemia developed SSIs versus 24% of patients with normal pre-operative albumin levels however this was not statistically significant ($p = 0.315$).

Patients receiving IMDs had fewer wound complications than those who did not (19.6% vs. 33%, $p = 0.049$) (Fig. 1). The significance of this association strengthened when benign diagnoses were excluded (24% vs. 43%, $p = 0.0005$). Sixty-one of the 89 SSIs (68.5%) resulted in considerable morbidity and required IV antibiotics, wound packing, hospital re-admission, negative pressure wound therapy, interventional radiology and/or operating room procedures. A subgroup analysis of patients who received IMDs indicated that they were significantly less likely to have wounds that incurred this type of morbidity (12% vs. 21%, $p = 0.03$) (Table 1). After controlling for significant covariates including ASA classification, BMI, history of diabetes mellitus or pelvic radiation, length of surgery, EBL and administration of TPN, consumption of Impact post-operatively remained protective against wound complications (OR 0.45, CI 0.25–0.84, $p = 0.013$) (Fig. 2). To determine the influence of Impact supplementation on the clinically morbid CDC SSI class 2 and 3 infections, we compared the rates of these two classes of SSIs in patients who did and did not receive post-operative IMDs. On