Brief Report

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Evaluating the Impact of Omega-3 Free Fatty Acid Supplementation on Postoperative Complications in Obese Postmenopausal Women With Estrogen Receptor Positive Breast Cancer

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Fish oil has beneficial effects in animal models with regards to wound healing time, prevention of infection, and decreased scar tissue formation.[1] The potential role of fish oil (omega-3 fatty acid) supplementation prior to breast cancer surgery has not been studied. There have been recent studies conducted to determine the potential preoperative benefits of fish oil supplementation. Despite the potential beneficial effects on wound healing, many still question the use of fish oil prior to undergoing surgery.

It has been previously hypothesized that supplementation with omega-3 fatty acids would result in an increased incidence of postoperative bleeding.[2] This once theorized complication greatly affected the ability of researchers to study the potential benefits of fish oil supplementation in patients undergoing surgical procedures.

According to a systematic review of 52 publications conducted by Begtrup et al, fish oil exposure in surgical patients does not increase bleeding or blood transfusion requirements either during or after surgery.[3] The study ultimately concluded that fish oil supplements were effective in reducing platelet aggregation in individuals. More importantly, they concluded that the observed biochemical effect of reduced platelet aggregation did not ultimately lead to an increase in bleeding risk during or after surgery.

Now that the once theorized intraoperative and postsurgical complications of omega-3 supplementation have been researched and rejected, it is of importance to explore the potential benefits of omega-3 supplementation in patients undergoing breast cancer surgery. For the purpose of this study, we hypothesized that obese postmenopausal patients with ER+ breast cancer undergoing breast surgery who consume omega-3 supplements 30 days prior to their surgery will experience a decrease in wound healing complications as well as surgical site infections (SSIs) compared to individuals who do not supplement with omega-3 prior to their procedures.

The objectives of this study were to assess the impact of omega-3 fatty acid supplementation on the incidence of surgical site healing complications (SSHCs) and SSIs in obese postmenopausal women with estrogen receptor-positive breast cancer undergoing surgery. Our study is part of a larger ongoing study that is being conducted at the Mays Cancer Center in San Antonio. We hypothesize that individuals who receive omega-3 fatty acids supplementation prior to undergoing breast surgery will have a lower incidence rate of both SSIs and SSHCs.

Our study utilized data from a larger study that was a prospective, comparative, 2 arm, short-term, interventional study with correlative biomarker endpoints. Patients were randomized to one of 2 arms of 100 patients each: letrozole 2.5 mg by mouth/daily (control) and omega-3 FFAs, 2700 mg by mouth twice daily + letrozole (test). All patients were treated with letrozole as a means of treating ER+ breast cancer during the 21-30 days prior to surgery. While a meaningful response to this treatment was not expected, this was included in our study design to mitigate concerns about the progression of disease as well as patient anxiety.

Patients were randomized to one of the 2 groups and were treated for 21-30 days before undergoing their

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POSTSURGICAL QUESTIONNAIRE

Date of surgery: ____/____/____

Date of completion: ____/____/____ *Should be completed **2 weeks from surgery date** (+7 days window allowed)*

Wound healing complication:	Circle One
Seroma	Yes No
Hematoma	Yes No
Delayed wound healing (3+ days)	Yes No
Partial Areola necrosis	Yes No
Complete areola necrosis	Yes No
Other:	

With regards to Surgical Site Infection (SSI) rate	Circle One
Superficial SSI	Yes No
Deep incisional SSI	Yes No
Organ/space SSI	Yes No
None	Yes No
Other:	

Print Name of Surgeon _____ Signature _____ Date Signed _____

Figure 1. Post-Surgical questionnaire.

surgery. A follow-up clinical exam was performed by a surgeon 2 weeks after surgery. The clinical exam included determining if any adverse events had occurred and the completion of a brief postsurgical questionnaire (Figure 1). The data were analyzed using a Fisher exact test.

Extensive data are available on omega-3 free fatty acid supplementation and positive impact on patient health, including tolerability and cancer-specific outcomes. The standard recommended dose of 1500 mg of docosahexaenoic acid and 2500 mg eicosapentaenoic acid given daily has been shown to decrease prostaglandin E2 production in healthy subjects.[4] as well as in our own 30-day feasibility study in postmenopausal obese women (n = 28, 74% demonstrating a decrease in serum PGE2 levels an average of 24%).

The patient population consisted of ER+ postmenopausal >30 BMI women (no chronic use of NSAIDS) scheduled for surgical resection 21-30 days from treatment start date (no washout period). The patient population was 64.5% Hispanic, 29% non-Hispanic whites, and 6.5% Black. Our study population had a median age of 60 years, and a median BMI of 32.18. The incidence of diabetes and hypertension was 16% and 39%, respectively (Table 1). 90% of our study population had a mastectomy (10% bilateral and 90% unilateral), and 10% underwent lumpectomy (Table 1).

There was a trend toward decreased surgical site healing complication and infection rate in patients who received omega-3 fatty acid supplementation (Table 2). The incidence of healing complications and infections was 8% in the omega-3 group (n = 25) compared to 33% in the control group (n = 6). This however was not statistically significant (P = .1594).

Although our study failed to show a statistical significant difference in postoperative wound healing complications, this is the first study evaluating omega-3 fatty acids in breast surgery. While we noted a trend of decreased SSHCs and SSIs with omega-3 supplementation. Our findings were limited by our small patient population size.

In summary, our study suggests that omega-3 fatty acid supplementation before breast surgery does not negatively impact healing. Our study highlights the need for further research into the beneficial aspects of omega-3 supplementation prior to undergoing breast cancer surgery as well as various other types of surgery. It may be of particular benefit to perform this study in a broader population of individuals who are undergoing elective surgery in which a 2-3-week period of omega-3 fatty acid supplementation may not deter potential candidates from enrolling in the study. It is also important to note that a larger sample size would increase the power of the study.

Table 1. Demographic Data.

	All patients (n = 31)	Fish oil (n = 25)	Control (n = 6)
Age, years	61.1 (49-88)	61.7	58.2
BMI	32.83 (22.7-41.8)	32.06	37.12
WT	83.93 (61.2-117.5)	83.37	100.13
DM (%)	16	20	0
HTN (%)	39	44	17
Smoking (%)	26	20	50
Race (%)			
Hispanic	65	68	50
Non-Hispanic	29	24	50
African American	6	8	0
Procedure type (%)			
Lumpectomy	10	12	0
Mastectomy	90	8	100
LN biopsy	100	100	100

Notes: n, number in group; BMI, body mass index (kilogram per meter squared) (0 = no, 1 = yes); WT, weight (kilogram); DM, diabetes mellitus (0 = no, 1 = yes); HTN, hypertension (0 = no, 1 = yes); race, (0 = no, 1 = yes), procedure type (0 = no, 1 = yes); LN, lymph node; biopsy (0 = no, 1= yes).

Table 2. Incidence of Wound Healing Complications and Surgical Site Infections.

	Yes	No	Total
Control	2	4	6
Omega-3	2	23	25
Total	**4**	**27**	**31**

Note: The incidence of healing complications and infections was 8% in the omega-3 group (n = 25) compared to 33% in the control group (n = 6). This however was not statistically significant (P = .1594).

In addition, we believe that it is of importance to research the effect of preoperative omega-3 fatty acid supplementation on alterations to the tumor microenvironment in obese postmenopausal individuals with ER + breast cancer, and this study is on-going.

Declaration of Conflicting Interests

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