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Chemotherapy Does Not Adversely Impact Outcome Following Post-Incisional Hernia Repair With Biomaterial Mesh

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Background: Patients receiving chemotherapy are at increased risk for developing recurrent or post-incisional hernias (PIH). Biological materials are an alternative to synthetic mesh in contaminated fields. The impact of chemotherapy on biomaterial tissue ingrowth and integration has not been well studied.
Methods: From 2008 to 2011 patients who underwent PIH repair with biomaterial mesh (Biodesign®) were selected. Patients were divided into two groups: those receiving chemotherapy (CT) and those not receiving chemotherapy (NCT).
Results: Forty-five patients were identified, 28 (62%) in the NCT group and 17 (38%) in the CT group. Median follow up for NCT and CT groups were 27 and 17 months, respectively. A total of 9/45 (20%) surgical site infections (SSI) were diagnosed, with 6/28 (21%) in the NCT and 3/17 (18%) in the CT group ($P = 0.53$). Seroma formation was seen in 5/28 (18%) of NCT patients and 4/17 (23%) in CT group ($P = 0.46$). Overall hernia recurrence rate was 22%, and the rates of recurrence were similar among the CT 3/17 (18%) and NCT 7/28 (25%) groups ($P = 0.42$).
Conclusion: The use of perioperative chemotherapy did not increase the rate of wound complications following PIH repair with biologic mesh in this group of patients.
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KEY WORDS: chemotherapy; post-incisional hernia repair; biological mesh

BACKGROUND

Post-incisional hernias (PIH) are a common complication after abdominal surgery. The incidence of ventral hernias after abdominal surgery ranges between 2% and 20% [1,2]. While PIH are usually asymptomatic; pain, incarceration, bowel obstruction, loss of abdominal domain, and strangulation can occur, often requiring surgical intervention. Higher risk of PIH has been associated with technical and patient-dependent factors. The type of abdominal incision, closure, and suture material used are among the technical factors associated with development of PIH [2]. Patient-dependent factors such as, obesity, gender, and immunosuppression also correlate with the risk of PIH [3,4]. Patients undergoing cancer treatment tend to develop PIH as a result of multiple and complex surgeries required for resection of underlying malignancy. Some patients require surgery in the context of perioperative chemotherapy, which places patients at higher risk of developing recurrent PIH and increased wound infections [5].

Synthetic mesh can be used in high-risk patients to repair and decrease the likelihood of PIH [3]. However, the risk of infection limits the use of synthetic mesh in contaminated cases. Infection of a synthetic mesh increases surgical morbidity and may require additional procedures for mesh explantation. Biological mesh products have emerged as an option to repair PIH in contaminated fields, with several products presently on the market. The user must appreciate that each biological prosthetic has unique properties and how these features may shape the indications and likelihood of success.

Biological materials such as, small intestine mucosa (SIS) incorporate into native tissue and function as scaffold for the ingrowth of vascularized tissue [6]. An advantage is the lower risk of infection and the potential to avoid removal even if infection develops, as they degrade in infected fields. The SIS extracellular matrix (ECM) consist of collagen and non-collagenous proteins and biomolecules including, glycosaminoglycans, proteoglycans, and glycoproteins. Upon implantation, host inflammatory cells and blood vessels infiltrate the graft. Connective and epithelial tissue growth and differentiation, as well as, deposition and maturation of the host ECM components occur. Finally, tissue remodeling takes place, in association with increased activity of immune cells including, CD4+ T lymphocytes [7]. We speculated that chemotherapy may suppress immune cell function and thus hinder the remodeling phase, increasing the risk of developing PIH following repair with biomaterial mesh. The incidence of PIH, SSI, and seroma formation after using biological mesh products in patients receiving chemotherapy has not been well defined.

Other authors have found no difference in rates of surgical wound complications and PIH recurrence when using a synthetic mesh compared to a biological mesh for PIH repair in patients immunosuppressed for reasons other than perioperative chemotherapy [8]. Moreover, in patients with gynecological malignancies receiving perioperative systemic chemotherapy, the use of biological mesh has been proposed as a prophylactic measure to prevent PIH [1]. The purpose of this study was to compare the rates of hernia recurrence, seroma formation, and wound infection following PIH repair with a biologic prosthesis in a contaminated field, among patients who received perioperative chemotherapy compared to individuals who did not receive chemotherapy.

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MATERIALS AND METHODS

This is a retrospective review of prospectively collected data of all patients who underwent elective, semi-emergent and emergent surgical repair of PIH in a contaminated field with biological mesh between January 1, 2008 and December 31, 2011 at Roger Williams Medical Center. All PIH repairs were performed with porcine SIS biomaterial mesh (Biodesign®, Cook Medical Bloomington, IN, US). After obtaining Institutional Review Board (IRB) approval, rates of PIH recurrence, SSI, seroma formation, and intra-abdominal abscesses requiring intervention were compared among patients receiving perioperative chemotherapy (CT group) and those not receiving chemotherapy (NCT group).

Contaminated or potentially contaminated fields were defined using Ventral Hernia Working Group (VHWG) grading system [9]. By the VHWG grading system, any patient with a previous wound infection, stoma present or violation of the intestinal tract is considered to have a potentially contaminated field or grade 3. Any patient with an infected mesh or septic dehiscence is considered as a grade 4 or contaminated field. Hernia recurrence was defined as a bulge or defect present at the repair site, confirmed by physical exam or computed tomography. Patients receiving the biomaterial mesh were followed up every 3 months for the first year and then every 6 months. If a hernia recurrence was suspected during the physical exam a computed tomography of the abdomen and pelvis was ordered and the event confirmed by an attending radiologist. All events were reviewed retrospectively by three authors.

Seroma was considered as any wound or intra-abdominal collection with no evidence of infection by physical exam or computed tomography. SSI was defined as those patients requiring antibiotics for wound erythema, postoperative opening of the surgical incision, percutaneous drainage, or operative debridement. Intra-abdominal abscess was defined as an intra-abdominal collection associated with fever, leukocytosis, and/or radiological signs of an infected collection and aspirate-growing bacteria.

Chemotherapy was considered to be perioperative if administered within 8 weeks of surgery. This window was chosen based on reports of wound complications seen up to 8 weeks after the use of Bevacizumab (AVASTIN, Genentech, San Francisco, CA) a vascular endothelial growth factor (VEGF) inhibitor, used in patients with metastatic colorectal cancer [10].

Three surgical oncologists within the same institution performed all PIH repairs. An intra-peritoneal underlay technique was used, the mesh was positioned with a minimum of 5 cm of overlap beyond the fascial edges. The defect in the fascia was re-approximated in all cases to reinforce the repair. Absorbable 1-PDS transfascial sutures were placed circumferentially, no more than 2 cm apart.

Data analysis was performed using SPSS (IBM Corp., Chicago, IL) using two tailed P values and a threshold for statistical significance set at <0.05. The Fisher's Exact test was used for data analysis where appropriate.

RESULTS

Forty-five patients who underwent PIH repair with SIS biomaterial were identified; 62% (28/45) patients belonged to the NCT group and 38% (17/45) to the CT group (Table I). There were 21 males and 24 females, with a median age of 61 (range 18–87). There was a non-significant trend toward older age in the CT group with a median age of 67 compared to 55 for the NCT group ($P = 0.07$). The median follow up was 27 months (range 3–36) for the NCT group and 17 months (range 2–43) for the CT group. Only two patients in the NCT group and three patients in the CT group had a follow up <12 months. The mean number of previous abdominal operations was two (range 1–5). The mean defect size in the NCT group was 8 cm (range 3–11) and in the CT group it was 9 cm (range 4–12) with no statistically significant difference between the groups. In the NCT group, 6 (21%) patients presented with incarcerated hernia, compared with 5 (29%) patients in the CT group ($P = 0.54$).

Co-morbidities in each group were also analyzed. In the NCT group, 28% (8/28) were smokers at the time of repair compared to 18% (3/17) in the CT group ($P = 0.32$). The body mass index (BMI) was also documented for each group, with a mean BMI of 28 (range 20–39) for the NCT group and 29 (range 15–39) for the CT group ($P = 0.67$). Twenty-one percent (6/28) of patients in NCT group and 29% (5/17) in the CT group had diagnosis of diabetes mellitus (DM) ($P = 0.54$).

In the CT group, the most common diagnosis was colorectal cancer, with 70% (12/17) of the patients with this diagnosis. Two patients had gastric cancer, two with ovarian cancer and one with pancreatic cancer. The most common chemotherapy received perioperatively was a combination of 5-fluorouracil, oxaliplatin, and leucovorin (FOLFOX) for colorectal cancer. Two patients also received Bevacizumab for colorectal liver metastatic disease. The patients with ovarian cancer received taxol and carboplatin; the patient with pancreatic carcinoma received gemcitabine; and the patient with gastric cancer received epirubicin, oxaliplatin, and fluorouracil.

All patients in the CT group had pre-existing ventral hernias that required emergent or semi-emergent surgery in the setting of systemic chemotherapy. Thirteen patients were classified as grade 3 and 4 patients as grade 4 by the VHWG grading system. Five of these 13 patients presented with incarcerated hernias requiring bowel resection, two presented with acute abdomen secondary to perforated appendicitis, one patient required open cholecystectomy for acute cholecystitis, and five patients presented with small bowel obstruction (SBO) that required exploration. The four patients classified as grade 4 required surgery for SBO. In the NCT group, 20 patients were classified as grade 3 and 8 patients as grade 4. Six patients had semi-emergent or emergent surgery for SBO secondary to incarcerated hernias, the other 22 patients had scheduled surgery for ventral hernia repair.

SSI was demonstrated in 21% (6/28) of patients in the NCT group and in 18% (3/17) of patients in the CT group ($P = 0.53$). Seromas were diagnosed in 18% (5/28) and 23% (4/17) of patients in the NCT and CT group respectively ($P = 0.46$). In the NCT group, two patients developed intra-abdominal abscesses that required image guided percutaneous drainage, while none in the CT group developed intra-abdominal abscess ($P = 0.38$). Hernia recurrence occurred in 25% (7/28) and 18% (3/17) of patients in the NCT and CT groups, respectively ($P = 0.42$, Fig. 1 and Table I). Two patients in each group had parastomal hernias, and an open intra-peritoneal mesh repair was used as described by Sugarbaker [11]. None of the hernia recurrences was seen in these patients. Most of the PIH repairs recurrences occurred within 12 months of the initial repair. The NCT group had a mean LOS of 4.9 days (range 1–26) and the mean LOS in the CT group was 7.6 days (range 1–16) ($P = 0.36$).

DISCUSSION

PIH is a well-known complication after abdominal surgery, particularly in cancer patients, with an incidence up to 20% [1]. Multiples factors contribute to the development of PIH and surgical site complications. Immunosuppression is a patient-dependent factor that has been associated with a higher incidence of PIH [5]. Synthetic products have been used for abdominal wall closure to decrease the incidence or recurrence of PIH repair. However, frequently patients undergoing major gastrointestinal surgery for malignancy are not suitable candidates for synthetic prostheses because of the risk of infection. Biologic products have emerged as an alternative option to treat and prevent recurrent PIH in contaminated fields. As patients with advanced abdominal malignancies often require systemic cytotoxic therapy, we undertook the present study to define the safety of biologic mesh in the context of perioperative chemotherapy.

TABLE I. Group Characteristics

Parameter	Non-chemotherapy group (NCT)	Chemotherapy group (CT)	*P*-Value
Number of patients (45)	28	17	
Median follow up (months)	27 (3–36)	17 (2–43)	
Median age	55 (18–85)	67 (36–87)	0.07
Males	14	7	0.39
Females	14	10	0.39
Mean defect size	8 (3–11)	9 (4–12)	0.28
Mean previous operations	2 (1–3)	2 (1–5)	0.42
Parastomal hernias	2 (7%)	2 (12%)	0.61
Incarcerated Hernias	6 (21%)	5(29%)	0.54
VHWG grading			
Grade 3	20 (71%)	13 (76%)	
Grade 4	8 (29%)	4 (24%)	
Co-morbidities			
Smoking	8 (28%)	3 (18%)	0.32
DM	6 (20%)	5 (29%)	0.54
BMI	28 (20–39)	29 (15–39)	0.67
Surgical site occurrences			
Seroma	5 (18%)	4 (23%)	0.46
SSI	6 (21%)	3 (18%)	0.53
PIH	7 (25%)	3 (18%)	0.42
LOS	4 (1–26)	6 (1–16)	0.36
Intra-abdominal abscess	2	0	0.38

SSI, surgical site infection; DM, diabetes mellitus; BMI, body mass index; PIH, post-incisional hernia; LOS, median length of stay; VHWG, ventral hernia working group grading system; Grade 3: previous wound infection, stoma present or violation of the intestinal tract; Grade 4: infected mesh or septic dehiscence.

The role of biologics as abdominal wall prosthetics in patients receiving perioperative chemotherapy is not well understood. Immunosuppressed patients may not mount the inflammatory response necessary for an effective remodeling phase of wound healing, impairing scar formation and tissue integration of the biomaterial [10,12]. Failure of mesh incorporation will limit the benefits of the biological abdominal wall prostheses and could increase surgical site complications.

The current study examined the use of lyophilized porcine small intestine submucosa (SIS) (Biodesgn®, Cook Medical, Bloomington, IN) in patients who received perioperative chemotherapy and required PIH repair. The choice of this particular mesh was based on our institutional experience as well as other reports documenting that SIS mesh remodels into vascularized host tissue [13–16]. The main indication for the use of SIS biomaterial mesh was a contaminated field during gastrointestinal tract surgery or previous wound infection. Other types of biologic mesh have been used in the setting of contaminated fields. Human acellular dermis (AlloDerm®) products have shown to be safe and effective for ventral hernia repairs in this setting [17,18]. The prospective repair of infected or contaminated hernias study (RICH study) evaluated the use of Strattice in contaminated fields. Strattice is a non cross-linked, porcine, acellular, dermal matrix that in high-risk patients allowed a single stage reconstruction of the abdominal wall in 70% of the patients, with a recurrence rate of 28% at 24 months [19].

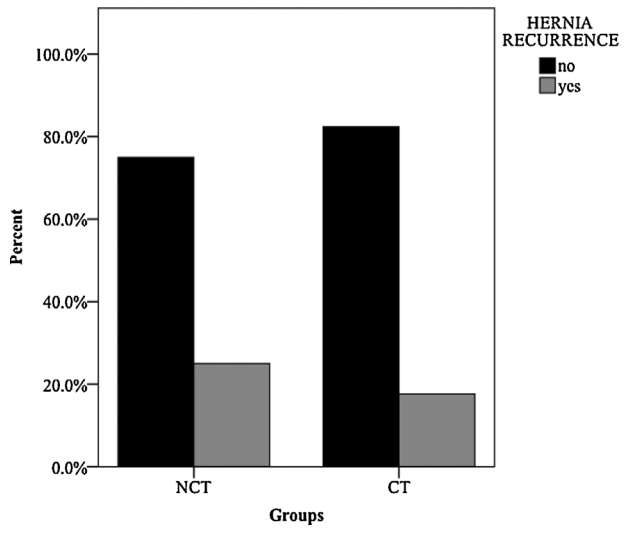

Fig. 1. Hernia recurrence per group after abdominal wall repair with SIS Biomaterial mesh. NCT 25% (7/28) versus CT 18% (3/17) ($P = 0.42$). CT, chemotherapy group; NCT, non-chemotherapy group; SIS, small intestine mucosa.

The incidence of superficial wound infection, seroma formation, and PIH were measured in the CT group and compared with the NCT group also requiring SIS biomaterial mesh for contaminated fields. We speculated that patients receiving perioperative chemotherapy would have a higher incidence of PIH due to impaired tissue incorporation into the biomaterial. No difference was seen between the two groups for recurrence ($P = 0.42$), seroma formation ($P = 0.46$) or surgical site infection ($P = 0.53$). We suspect that the use of the SIS biomaterial mesh, and its incorporation into native tissues, is not affected significantly by chemotherapy agents. Facilitation of scar formation seems to happen even in patients receiving chemotherapy, decreasing the number of expected hernias. This is even more surprising given that patients in the CT group tended to be older and were more likely to have undergone urgent repair.

The exact mechanism of mesh integration in immunosuppressed patients is not well understood, and further basic science research will be necessary to better understand how perioperative chemotherapy influences the wound healing process and incorporation of biologic mesh. Interestingly, there was no difference in surgical site infection or seroma formation rate between the CT and the NCT group. This suggests that chemotherapy in patients receiving SIS biomaterial does not increase wound morbidity and represents a viable option in elective, semi-emergent, and emergent cases. Two intra-abdominal abscesses were seen, both in the NCT group, though this could be because of the smaller sample size in the CT group. Also, the median follow up time in the CT group was shorter since some patients had succumbed to their cancer.

Similar findings have been reported in solid organ transplant patients, though using a different biological mesh. Other authors have demonstrated decreased rates of wound infections, PIH and need of mesh removal with biologic mesh when compared with synthetic mesh or primary repair in immunosuppressed patients [20]. Rettenmaier et al. [5] published a series of 1,391 patients with gynecologic malignancies that developed PIH. Chemotherapy, radiation therapy, and co-morbidities were associated with PIH and were predictors of early hernia recurrences. Their results support a more aggressive approach in cancer patients receiving chemotherapy or radiation therapy to prevent PIH, using synthetic mesh in non-contaminated fields or biological products in contaminated fields to prevent PIH.

The small sample size is an important limitation of our study, and the small differences noted in recurrence rates and complications may be found to be statistically significant with a larger sample size. In our series the only biological mesh used was the SIS biomaterial mesh (Biodesign®, Cook Medical, Bloomington, IN). However, analysis of the alternative biologic materials options is warranted to confirm our findings. Due to their different source and tissue integration, generalizations cannot be made about all biologic products. Further examination of cost-effectiveness would also be helpful to guide our decision making process about the use of biological products for abdominal wall closure in high-risk patients. The higher cost of biologic products should be weighed against the potential savings from a potentially lower risk of complications and reoperation.

CONCLUSION

The use of SIS biomaterial mesh has a potential role in abdominal wall closure of patients with PIH in the context of perioperative chemotherapy. The incidence of surgical site infection, seroma formation, recurrence, and intra-abdominal abscess after using SIS biomaterial mesh was not significantly different in the patients receiving perioperative chemotherapy compared to a control group. Further studies are required to expand our understanding of the various biological meshes that could be used under these settings.

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