

TITLE: Comparison Between Wound Vacuum Dressing and Standard Closure to Reduce Rates of Surgical Site Infections

NCT: NCT03021668

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JHM IRB - eForm A – Protocol

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1. Abstract

- a. Provide no more than a one page research abstract briefly stating the problem, the research hypothesis, and the importance of the research.

Although pancreaticoduodenectomy (PD) outcomes have improved, it remains a procedure with a high perioperative complication rate. Surgical site infection (SSI) is one of the most common complications after PD. In a retrospective review of all patients who underwent PD at Johns Hopkins between 9/2011-8/2014, a total of 679 patients, 30-day SSI was observed in 16.7%. By univariate analysis, perioperative blood transfusion, operative time greater than 7 hours, pre-operative chemotherapy and/or radiation, bile stent, absence of a superficial wound vacuum closure device, and vascular resection were associated with SSI (all, $p < 0.05$). On multivariable analysis, pre-operative bile stent/drain and neoadjuvant chemotherapy were independent predictors of SSI (all, $p < 0.001$). Studies in colorectal patients have found an estimated cost of up to \$1400 per patient secondary to prolonged hospitalization, wound care, and wound complications in patients with procedures complicated by a SSI. Furthermore, in another study of 1144 patients undergoing PD between 1995 and 2011 at Johns Hopkins Hospital, post-operative complications delayed time to adjuvant therapy, decreased median survival.¹

Our hypothesis is that placement of Prevena Peel & Place Dressing using the standard KCI VAC after suture on patients undergoing PD at highest risk of infection will result in a significant decrease in SSI rate. We plan to perform a randomized control trial where patients who have had pre-operative bile stent/drain placement and/or neoadjuvant chemotherapy will undergo closure with Prevena Peel & Place Dressing using the standard KCI VAC after suture versus standard closure. We will then follow these patients for 30 days post-operatively to determine SSI and other peri-operative complication rate.

2. Objectives (include all primary and secondary objectives)

Primary objective:

To evaluate the effectiveness of Prevena Peel & Place Dressing using the standard KCI VAC after suture closure versus standard closure at reducing wound infections in patients undergoing pancreaticoduodenectomy

Secondary objective:

To evaluate the impact of Prevena Peel & Place Dressing using the standard KCI VAC after suture on hospital length of stay, readmission, and time to adjuvant therapy

3. Background (briefly describe pre-clinical and clinical data, current experience with procedures, drug or device, and any other relevant information to justify the research)

Although pancreaticoduodenectomy (PD) outcomes have improved, it remains a procedure with a high perioperative complication rate. Surgical site infection (SSI) is one of the most common complications after PD. In a retrospective review of all patients who underwent PD at Johns Hopkins between 9/2011-8/2014, a total of 679 patients, 30-day SSI was observed in 16.7%. By univariate analysis, perioperative blood transfusion, operative time greater than 7 hours, pre-operative chemotherapy and/or radiation, bile stent, absence of a superficial wound vacuum closure device, and vascular resection were associated with SSI (all, $p < 0.05$). On multivariable analysis, pre-operative bile stent/drain and neoadjuvant chemotherapy were independent predictors of SSI (all, $p < 0.001$). Studies in colorectal patients have found an estimated cost of up to \$1400 per patient secondary to prolonged hospitalization, wound care, and wound complications in patients with procedures complicated by a SSI. Furthermore, in another study of 1144 patients undergoing PD between 1995 and 2011 at Johns Hopkins Hospital, post-operative complications delayed time to adjuvant therapy, decreased median survival.¹

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Our institution has extensive experience with using this product for the prevention of SSI in patients undergoing surgery over the past several years, most specifically after ventral hernia repair. Superficial wound vacuum closure has been shown in a previous study by our group to decrease SSI from 32% to 9% ($p < 0.001$) and surgical site occurrence (SSO) from 42% to 17% ($p < 0.001$) in patients undergoing ventral hernia repair. Furthermore, when used in grade 3 ventral hernias, superficial wound vacuum closure had an SSI rate of 5.2% and an SSO of 20.7% at 90 days, which is lower than previously published rates using standard closure in these complex hernia repairs. All surgeons who will participate in this study have familiarity with the use of the wound vacuum device after surgical closure.

4. Study Procedures

- a. Study design, including the sequence and timing of study procedures (distinguish research procedures from those that are part of routine care).

All patients who are planned to undergo pancreaticoduodenectomy at Johns Hopkins Hospital will be assessed for eligibility and enrolled. Members of the department of surgery who are listed as the team members will be responsible for approaching the participants. Patients will be screened for eligibility. Only patients who have received neoadjuvant therapy and/or have undergone biliary stent placement will be approached. In addition patients will also be screened for known allergies to silver or acrylic adhesives.

Date: April 10, 2018

Principal Investigator: Matthew J. Weiss

Application Number: IRB00109564

Recruitment will take place in the (i) surgical clinics, or (ii) at the pre-operative evaluation clinics prior to the surgery. Recruitment process will be mindful of patient privacy issues.

Discussions will be held by the potential participant's clinical and will not likely involve any additional patient protected health information beyond what is already required for the standard medical care. A written consent will be taken from these patients. The patients who are suitable candidates for the study will be approached in a clinical setting that is surgical clinics, preoperative assessment clinics, etc.

Those members of the research team (principal investigator, co-investigator, research nurse) who consent patients have been trained in informed consent procedures, are familiar with the protocol, and are listed as a consentor in the application document. Patients are given adequate time and privacy to consider the research study. Before the patient signs the consent, the consentor must be satisfied that the participant understands the information provided, has had an opportunity to discuss the information and ask questions, and is aware that he/she may withdraw from the study at any time.

A copy of the signed consent form will be provided to the patients at time of consent. Contact information will be provided to these patients so that they can contact the study team in the future, if they have any questions regarding the study.

Once consented, these patients will be entered into CRMS.

All consented patients will undergo the same standard PD. At the time of closure the patients will be randomized to either standard closure or closure using the Prevena Peel & Place Dressing using the standard KCI VAC after suture closure.

The device will be left in place for 4 days after surgery. As part of the patients' clinical evaluation the surgical wound site will be inspected daily by the surgical team. If there are signs of infections the device will be removed. All patients will have their device removed prior to discharge.

The patients will be evaluated for wound infection during their hospital stay and also during their outpatient follow-up for up to 30 days after surgery. The CDC guidelines will be used to diagnose SSIs.

All patients will be followed for 30 days to collect data on SSI and other post-operative complications.

In total we plan to consent 144 patients for this study – 72 patients in the Prevena Peel & Place Dressing using the standard KCI VAC after suture closure arm, and 72 patients in the standard control arm.

b. Study duration and number of study visits required of research participants.

The study duration will be approximately 2 years. The patients will not require additional research visits.

5. Inclusion/Exclusion Criteria

Inclusion Criteria:

1. Patient to undergo pancreaticoduodenectomy for a pancreatic tumor at the Johns Hopkins Hospital
2. Patient treated with neoadjuvant chemotherapy with or without radiation therapy prior to surgical resection, AND/OR placement of a biliary stent and/or drain for biliary tree decompression

Exclusion Criteria:

1. Age 18 years or younger
3. Laparoscopic or robotic pancreaticoduodenectomy
4. Patient did not undergo either placement of a preoperative biliary stent/drain or neoadjuvant chemotherapy with or without radiation therapy.
5. All patients who are have known allergies or are sensitive to silver and acrylic adhesives.

6. Drugs/ Substances/ Devices

- a. The rationale for choosing the drug and dose or for choosing the device to be used.
Our institution has extensive experience with using this product for the prevention of SSI in patients undergoing surgery over the past several years, most specifically after ventral hernia repair. Superficial wound vacuum closure has been shown in a previous study by our group to decrease SSI from 32% to 9% ($p < 0.001$) and surgical site occurrence (SSO) from 42% to 17% ($p < 0.001$) in patients undergoing ventral hernia repair. Furthermore, when used in grade 3 ventral hernias, superficial wound vacuum closure had an SSI rate of 5.2% and an SSO of 20.7% at 90 days, which is lower than previously published rates using standard closure in these complex hernia repairs.

7. Study Statistics

- a. Primary outcome variable.
The primary outcome variable is surgical site infection (SSI) rate
- b. Secondary outcome variables.
The secondary outcome variables are hospital length of stay, readmission rate, and time to adjuvant chemotherapy
- c. Statistical plan including sample size justification and interim data analysis.
The primary outcome variable, SSI rate, will be analyzed using a chi-square test. The secondary outcome variable of hospital length of stay will be analyzed using a t-test if the data are normally distributed or a ranksum test if they are not. The secondary outcome variable of readmission rate will be analyzed using a chi-square test. The secondary outcome variable of time to adjuvant chemotherapy will be analyzed using survival analysis methods, including Kaplan-Meier curves and log-rank test.

Prior data from our institution has demonstrated that the risk of a surgical site infection after pancreaticoduodenectomy is 30% if the patient either underwent neoadjuvant chemotherapy or had a biliary stent/drain placed before surgery. This study has been powered to show a decrease in SSI rate from 30% to 10%, and thus would necessitate 72 patients in each arm of the trial (Open Epi software, with Fleiss continuity correction).

Interim data analysis will only performed to monitor for futility, as described below.

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d. Early stopping rules.

We will perform an interim analysis when SSI results are available for the first 36 patients in each group. Conditional power calculations will be performed according to the method proposed by Proschan, Lan, and Wittes (2006), assuming that the results seen up until the interim analysis continue until the end of the trial (empirical conditional power). If the conditional power under the empirical assumption is less than 0.50, the trial will be terminated for futility.