Efficacy of Negative Pressure Wound Treatment in Preventing Surgical Site Infections after Whipple Procedures

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Surgical site infections (SSIs) occur at an average rate of 21.1 per cent after Whipple procedures per NSQIP data. In the setting of adherence to standard National Surgery Quality Improvement Program (NSQIP) Hepatopancreatobiliary recommendations including wound protector use and glove change before closing, this study seeks to evaluate the efficacy of using negative pressure wound treatment (NPWT) over closed incision sites after a Whipple procedure to prevent SSI formation. We retrospectively examined consecutive patients from January 2014 to July 2016 who met criteria of completing Whipple procedures with full primary incision closure performed by a single surgeon at a single institution. Sixty-one patients were included in the study between two cohorts: traditional dressing (TD) (n = 36) and NPWT dressing (n = 25). There was a statistically significant difference ($P = 0.01$) in SSI formation between the TD cohort (n = 15, SSI rate = 0.41) and the NPWT cohort (n = 3, SSI rate = 0.12). The adjusted odds ratio (OR) of SSI formation was significant for NPWT use [OR = 0.15, $P = 0.036$] and for hospital length of stay [OR = 1.21, $P = 0.024$]. Operative length, operative blood loss, units of perioperative blood transfusion, intraoperative gastrojejunal tube placement, preoperative stent placement, and postoperative antibiotic duration did not significantly impact SSI formation ($P > 0.05$).

THE WHIPPLE PROCEDURE (pancreaticoduodenectomy) is the only potential curative treatment for pancreatic cancer. Per NSQIP data, pancreatic surgery is associated with numerous complications, with an overall rate of 51 per cent. Total surgical site infection (SSI) rates per NSQIP are 21.1 per cent including a 7.1 per cent superficial SSI rate, 2.3 per cent deep incisional SSI rate, and 11.37 per cent organ space SSI rate. Pancreatic fistulas (PF)—which also usually result in deep SSI formation—occur at a rate of 18.1 per cent. Patients undergoing Whipple procedures are most commonly in their 60s, and are often in poor health with multiple comorbidities resulting in average American Society of Anesthesiologists scores of 3 to 4.[1] The traditional open operation involves a large midline incision that can extend from the xiphoid process to below the umbilicus. Operative time is often six hours or greater, and intraoperative blood loss averages between 500 and 1400 mL, with an average of 1 to 1.5 units of blood transfusion needed.[1] Postoperative hospital length of stay (LOS) ranges between 1 and 2 weeks on average with a mean of 13 days.[1, 2] Nutritional status is also often difficult to maintain in these patients, particularly in the presence of delayed gastric emptying. Each of these elements is independently associated with increased incidence of SSI and collectively are why SSIs are a top postoperative complication after the Whipple procedure.

The Centers for Disease Control defines SSIs as being either superficial or deep. Superficial SSIs are defined by positive wound culture findings and/or clinical evidence of infection not limited to site tenderness, erythema, pustular drainage, and systemic signs such as fever. Deep or organ space SSIs are characterized by evidence of infection through one of the deeper layers of the incision. This includes findings such as intra-abdominal abscesses with fluid that may require drainage. Despite this clear breakdown of SSI types, in clinical practice, there is some difficulty with specifically characterizing an SSI as deep *versus* superficial. Without routine CT, it can be difficult to identify an infection as a superficial or as a deep infection that simply expressed itself through the surface incision.

One of the more recent, promising developments in postoperative incision wound care is the use of

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modified negative pressure wound treatment (NPWT). These devices have a pad that can be sterilely applied over the site of the incision and adhered to the skin at the perimeter to create a sealed environment around the wound. The pad is then attached to a handheld pump to create negative pressure within the sealed area. This device is notably different than larger conventional wound vacuums which have been available for years. These larger wound vacuums are attached to a canister and generally require custom cut foam insertion into the wound site. Large wound vacuums are better equipped to handle large open wounds with high quantity exudate. However, these machines are considerably more expensive and inconveniently used in the outpatient setting because they require frequent dressing changes of the foam inserts. On the other hand, the smaller NPWT devices being discussed in this manuscript have a life span of one week, use lower pressure settings, are much cheaper and more portable, and can be applied over closed incisions for a prophylactic use.

There have been a number of large-scale studies that have shown the efficacy of NPWT in decreasing wound complications in open or previously infected wounds. On the other hand, there has been much less published about the use of NPWT over closed incision sites with the goal of prophylactically preventing SSIs. Whereas there have been no studies demonstrating the use of prophylactic NPWT after Whipple procedures, a few smaller studies have shown benefit of prophylactic NPWT use after orthopedic, colorectal, vascular, plastics, cardiothoracic, and trauma procedures.[3, 4]

Methodology

With Institutional Review Board approval, we retrospectively examined consecutive patients from January 2014 to July 2016 who met the criteria of completing a Whipple procedure with full primary incision closure performed by a single surgeon at a single institution. Standard recommendations for SSI reduction were used in all cases (wound protector, glove change prior to closure, perioperative antibiotics). The same brand NPWT was placed at the end of each procedure for those patients in the NPWT cohort and was left in place for 7 to 10 days. Superficial infections were categorized based on clinical findings. All deep infections were thus categorized based on CT evidence of a fluid collection or abscess below the fascia. Mixed infections had evidence of deep infection but also clinical findings of a superficial infection. Data were analyzed with two-tailed *t* test, and multivariate logistic regression analysis (IBM SPSS Version 2, Armonk, NY) was used to evaluate risk factors for SSIs.

Results

Sixty-one patients were included who were divided between two cohorts: traditional dressing (TD) (n = 36) and NPWT dressing (n = 25). The cohorts were not significantly different in age (TD = 64.1 years; NPWT = 61.1 years), smoking history (TD = 22%; NPWT = 20%), significant alcohol history (TD = 22%; NPWT = 36%), body mass index (TD = 26%; NPWT = 24%), preoperative stent placement (TD = 44%; NPWT = 48%), operative length (TD = 461 minutes; NPWT = 504 minutes), operative estimated blood loss (TD = 529 mL; NPWT = 510 mL), intraoperative GJ tube placement (TD = 33%; NPWT = 12%), postoperative antibiotic treatment (TD = 100%, NPWT = 100%), hospital LOS (TD = 12.9 days; NPWT = 12.1 days) (see Table 1). There was a significant difference ($P = 0.01$) in SSI formation between the TD cohort (41%, $n = 15$) and the NPWT cohort (12%, $n = 3$). Among the TD cohort SSIs, nine were deep, four were mixed, and two were superficial. Among the NPWT cohort SSIs, two were mixed and one was deep (see Fig. 1). PF were associated with six of the TD cohort SSIs and two of the NPWT SSIs (TD PF rate = 17%, NPWT PF rate = 8%; $P = 0.33$). Of the total PF, clinically significant grade B PF was associated with four of the TD cohort SSIs and two of the NPWT SSIs (grade B TD PF rate = 11.1%, grade B NPWT PF rate = 8%; $P = 0.69$). The number needed to treat, defined by the number of patients who would need to be treated with NPWT to prevent one SSI, was 3.4. Multivariate regression was performed to evaluate risk factors for SSI formation. There were two factors that were statistically correlated with SSI formation. There was negative correlation between SSI formation and use of NPWT [OR = 0.15, $P = 0.036$] and positive correlation between SSI formation and length of hospital stay [OR = 1.21, $P = 0.024$]. Operative length, operative blood loss and blood transfusion, GJ tube placement, preoperative stent placement, and postoperative

TABLE 1. *Cohort Comparison*

	TD	NPWT	*P* value
SSI (%)	0.41	0.12	$P = 0.01$
Body mass index (kg/m^2)	25.7	24.2	$P = 0.23$
Operative Length (min)	461.4	504.6	$P = 0.14$
EBL (mL)	529.2	510.2	$P = 0.84$
Intraoperative Blood Transfused (units)	0.67	0.4	$P = 0.31$
Intraoperative GJ Tube Placement (%)	0.33	0.12	$P = 0.07$
Preoperative Stent Placement (%)	0.44	0.48	$P = 0.79$
LOS (days)	12.9	12.14	$P = 0.646$
Smoking History (%)	0.22	0.20	$P = 0.83$
Alcohol History (%)	0.22	0.36	$P = 0.24$

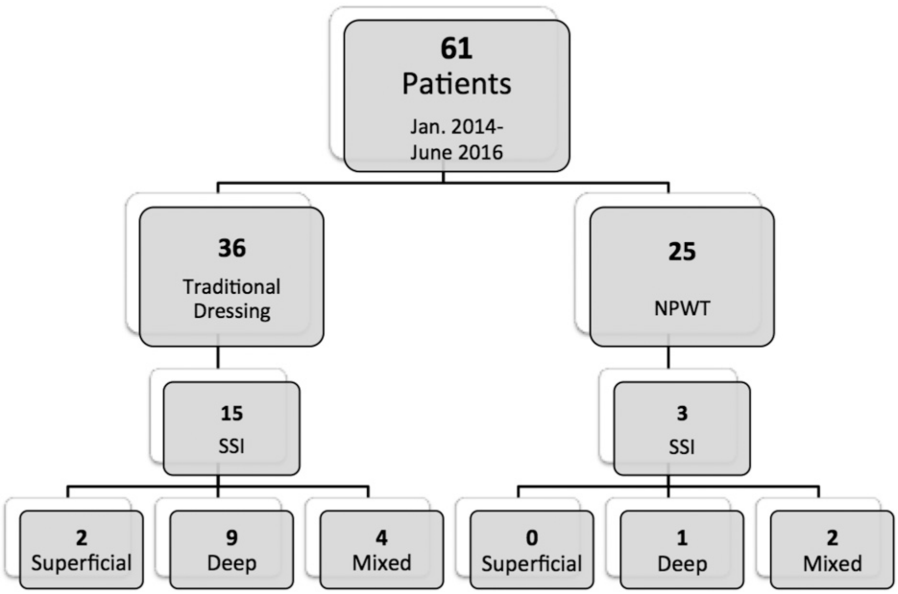

FIG. 1. Cohort outcomes.

antibiotic duration were not significantly correlated with SSI formation ($P > 0.05$).

Discussion

The data demonstrate a statistically significant decrease in SSI when comparing the TD cohort with the NPWT cohort. This study is unique in its cohort size as well as in its focus of evaluating NPWT efficacy specifically after Whipple procedures requiring midline incisions. Although other studies have shown NPWT efficacy of infected or high-risk wounds, this is the first study to demonstrate that the prophylactic use of a NPWT after a Whipple procedure is effective in reducing SSI incidence.

The underlying mechanism of NPWT's effect is hypothesized to occur in three primary ways. First, the sealed negative pressure whisks away excess edema-forming interstitial fluid and reduces inflammatory mediators around the wound; studies have shown decreased C-reactive protein, TNF-α, and Il-6 levels in tissue treated with NPWT compared with TD.[5] The second major effect of NPWT is enhanced blood flow and angiogenesis. This promotes more effective healing with improved oxygenation, cellular proliferation, and migration of wound healing factors. Cutaneous blood flow has been shown to increase 3 to 5× in tissue treated with NPWT.[6] Improved cell-mediated response and T-cell migration results in bacterial colony counts shown to be decreased in NPWT cohorts compared with TD controls.[7] This also allows for the top down effect by which deeper infections are prevented with NPWT use: essentially by decreasing superficial bacterial colonization, less bacteria are able to migrate down to the deeper layers of the surgical site and contribute to infection in those areas. Whereas the NPWT does not decrease the incidence of PF or prevent infection that originates intra-abdominally, this top down effect could theoretically explain the reduction in deep infections between the two cohorts that our data demonstrated. Finally, the negative pressure also creates favorable biomechanics for wound healing. The negative pressure increases strain at the wound's tissue edge which further increases cell proliferation and wound healing via increased levels of collagen, VEGF, and FGF-2 in NPWT treated rat tissue.[8] It also promotes wound healing by reducing tensile forces and ultimate stress across the wound by up to 50 per cent.[9]

In addition to being effective because of these factors, the NPWT is also economically sustainable. The burden of SSI on the United States healthcare system is staggering with costs cited of up to $10 billion annually in direct and indirect costs. Schweizer et al.[10] found in a study of the VA system that the cost can be up to $25,721 greater when treating a patient who develops an SSI *versus* one who does not. Shepard et al.[11] evaluated costs of SSI at Johns Hopkins over a three-year period and found that the costs of SSI to the hospital came out to over $12 million dollars over that period, averaging a cost of $19,683 per SSI to the hospital. The financial burden of SSI to hospital systems is amplified by the fact that many payers, including Medicare, will usually not reimburse most of the costs associated with an SSI related readmission. These immense financial costs to the hospital in addition to patient SSI-related mortality and morbidity can be weighed against the cost of a NPWT—which on average costs $851 according to one major NPWT manufacturer. Thus, given the enormous potential for cost benefit and improved patient outcomes, the standard prophylactic use of NPWT over all closed incision sites to decrease SSI incidence should be considered.

However, a large scale, multispecialty, hospital-wide randomized, controlled study is still lacking. A large scale study that replicates results similar to this study and some of the others that have been published regarding NPWT in other specialties would not only increase providers' confidence in NPWT's efficaciousness but would be an important step to securing Medicare and other payer reimbursement for prophylactic postoperative NPWT use. Other studies to optimize NPWT protocol including pressure settings and length of use are also needed.

The prophylactic use of NPWT over closed incision sites is an exciting development in the standard of wound postoperative wound care. By decreasing swelling and inflammation, increasing incisional blood flow and immune factors, and optimizing wound biomechanics, the NPWT has the potential to decrease SSI. Our data demonstrate a significant reduction in SSI among the NPWT cohort while accounting for confounding operative and patient variables. Whereas large-scale randomized controlled trial studies on the topic are warranted, NPWT should be considered over TD for SSI prophylaxis—particularly after surgeries highly associated with SSI formation such as the Whipple procedure.

Note added in proof: *A recent phase II randomized trial in patients undergoing laparotomy for abdominal malignancies treated postoperatively with four days of NPWT failed to show a reduced rate of SSIs after Whipple procedures [Shen P, Blackham AU, Lewis S, et al. Phase II Randomized Trial of Negative-Pressure Wound Therapy to Decrease Surgical Site Infection in Patients Undergoing Laparotomy for Gastrointestinal, Pancreatic, and Peritoneal Surface Malignancies. J Am Coll Surg. 2017;224(4):726–737.]*

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