Dressings for Wound Infection Prophylaxis in Colorectal Surgery: A Review

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ABSTRACT

ntroduction: In patients who require colorectal surgery, the rate of surgical site infection (SSI) is amongst the highest of any surgical specialty. Guided by the enhanced recovery after surgery (ERAS) guidelines for colorectal surgery, there is a large focus on preoperative and intraoperative measures to reduce the risk of bacterial transmission and surgical site inoculation There are many novel and developing dressing types being explored for colorectal surgery. To date, no consensus guidelines for surgical dressings that optimize healing outcomes and reduce infection from postoperative incisions have been established. The purpose of this review is to discuss various dressings used for surgical site wound infection prophylaxis for patients who have colorectal surgery.

<u>Materials and Methods</u>: The database, PubMed, was used for this literature review. Keywords included: colorectal surgery or abdominal surgery or clean-contaminated surgery + surgical site infection prophylaxis or negative-pressure wound therapy or bandages or biological dressings or occlusive dressings + surgical wound infection.

<u>Results:</u> Five prophylactic dressings were selected for discussion. This article will review current use and research surrounding the utilization of negative pressure wound therapy devices, silver-containing dressings, mupirocin dressings, gentamicin-c sponge, and vitamin- e and silicon sponges.

<u>Conclusion</u>: Alternative dressings discussed in this article show significant promise in reducing SSI compared to conventional dressing. Additional studies to assess cost-benefit analysis and integration into general practice are needed to determine practical application.

INTRODUCTION

There is a multitude of factors that contribute to why a wound becomes infected. Among these factors exist those which may be accounted for and controlled, while other variables may not be controlled or are yet to be determined. Surgical technique, which is up to the individual surgeon and their surgical team, is one of the largest contributing factors to surgical site infection (SSI). Maintenance of clean wound edges, hemostasis, adequate perfusion to the skin, and vigorous irrigation of contamination are all factors that may be recognized and controlled. Whereas variables related to the individual patient, such as various states of compromised immunity attributed to medications or disease states, are difficult to control.

In patients who require colorectal surgery, the rate of SSI is amongst the highest of any surgical specialty. SSI rates vary from 4-26%.1-3 In colorectal surgeries, a high infection rate is due in part to the high bacterial load within the colon and rectum. The surgical wound classification (SWC) is categorized by the degree of gross contamination: clean, clean-contaminated, contaminated, or dirty (Table I), and is used in conjunction with the ASA and procedure duration to identify those at risk of SSI.⁴ In colorectal surgery, if the surgical procedures are carried out with skilled technique, and in the absence of pre-existing local infection, the operation is considered a clean-contaminated operation-the majority of elective colorectal cases fall under this category. If during the operation fecal spillage occurs, then the operation is considered contaminated. At this point, the risk of SSI is dependent on the dose and virulence of contaminating microorganisms and the level of resistance of the patient.⁵

The American College of Surgeons (ACS) reviewed nearly 50,000 surgical procedures which revealed that major contributors to SSI development included the following: dependent functional status; obesity; emergency nature, complexity, or longer duration of surgical procedure; respiratory conditions limiting perfusion; diabetes; smoking; coronary artery and peripheral vascular disease; coagulopathy; female sex, and preoperative sepsis.⁶ Identifying the risk factors for SSI allows for a more educated and proactive approach, which may minimize any delay in healing. Dressing selection plays a key role in post-surgical incision care to protect the wound and avoid surgical wound complications. Dressing selection is highly variable and surgeon dependent. Dressing options range from classically used gauze to more modern hydrogels, hydrocolloids, alginates, foams, films, and negative pressure options.

Interventions to reduce the rate of SSIs in colorectal surgery are necessary to optimize both patient care and medical costs. While wound infection is rarely lifethreatening, it may prolong hospital stays, increase medical costs, and adversely impact a patient's quality of life.^{7, 8} First established in 2005, enhanced recovery after surgery (ERAS) guidelines for col-

Table I Surgical wound classification grades as defined by the CDC					
Class I <i>Clean</i>	An uninfected operative wound in which no inflammation is encounter and the respiratory, alimentary, genital, or uninfected urinary tract is n entered. In addition, clean wounds are primarily closed and, if necessa drained with closed drainage. Operative incisional wounds that follow nonpenetrating (blunt) trauma should be included in this category if th meet the criteria.				
Class II Clean-contaminated	An operative wound in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination. Specifically, operations involving the biliary tract appendix, vagina, and oropharynx are included in this category, provided no evidence of infection or major break in technique is encountered.				
Class III Contaminated	Open, fresh, accidental wounds. In addition, operations with major breaks in sterile technique (e.g., open cardiac massage) or gross spillage from the gastrointestinal tract, and incisions in which acute, <u>nonpurulent</u> inflammation is encountered are included in this category.				
Class IV Dirty-infected	Old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera. This definition suggests that the organisms causing postoperative infection were present in the operative field before the operation.				

orectal surgery focus on perioperative protocolization to reduce postoperative complications, in an effort to reduce wound infections and maximize patient outcomes. These guidelines suggest a reduction in alcohol consumption, smoking cessation, anemia management, preoperative nutritional management, antimicrobial prophylaxis, skin preparation, prevention of postoperative nausea and vomiting, and early ambulation among many other recommendations.⁹ The ERAS guidelines are constantly evolving with the incorporation of novel techniques or tools as evidence suggests patient outcome benefits. Both intraoperative wound protection devices¹⁰⁻¹² and triclosan-coated sutures are interventions that have demonstrated reduced SSI after colorectal surgery.^{13,14} Yet, neither device is currently recommended under ERAS guidelines.

Many novel and developing dressing types are being explored for colorectal surgery. To date, there has not been a consensus on the establishment of guidelines for surgical dressings that focus on the optimization of healing outcomes and reduction in infections from postoperative incisions. This article is not meant to be a comprehensive review of the causes and prevention measures for all types of SSI. Instead, the purpose of this review is to discuss various dressings used for surgical site wound infection prophylaxis in patients who have colorectal surgery while exploring one technical aspect that could aid in the decrease of a worldwide surgical problem. Table II provides an overview of the article findings, dressing indications, and consensus of dressing use in clinical practice.

MATERIALS AND METHODS

The following terms were searched on PubMed: colorectal surgery, abdominal surgery, clean-contaminated surgery plus surgical site infection prophylaxis, negative-pressure wound therapy or bandages, biological dressings, and occlusive dressings plus surgical wound infection. Following review, five prophylactic dressings were selected for discussion.

RESULTS

Negative pressure wound therapy devices

Negative pressure wound therapy (NPWT) has been used since the 19th century for wound care¹⁵ and has more recently been tested as a means of SSI prophylaxis. NPWT is a broad term used to describe a unique and versatile system that aids the optimization of wound healing through the application of sub-atmospheric pressure to help reduce inflammatory exudate and promote granulation tissue. Negative pressure wound therapy is primarily utilized to treat complex wounds which are non-healing or at risk of non-healing. In recent years, NPWT has been adapted for the adjunctive treatment of closed wounds, such as closed surgical incisions. Of the discussed novel dressings in this article, NPWT is by far the most researched for colorectal infection prophylaxis.

NPWT is indicated for acute wounds when the wound cannot be closed by primary intention due to the risk of infection, active infection, skin tension, or swelling.¹⁶ It is thought to promote wound healing by providing a warm, moist wound bed while removing wound fluid through negative pressure. This removes molecular factors that inhibit cell growth, improves blood flow to the wound, enhances wound oxygenation, and improves the flow of nutrients to the wound. NPWT may also create mechanical forces that influence the wound macroscopically, by drawing the wound edges together, and microscopically, by exerting mechanical forces on tissue that induces cell proliferation, cell migration to the wound, and angiogenesis.

Bonds et al., in a retrospective study in 2013, were the first to investigate the use of NPWT in colorectal surgery.¹⁷ Although a considerable number of studies have found that NPWT decreases the SSI rate,¹⁸⁻²² other research has found no relationship between NPWT use and SSI rate.²³ Notably, the NEPTUNE trial, a randomized controlled trial (RCT) assessing prophylactic use of NPWT on primarily closed incisions after open colorectal surgery, found no significant reduction in the rate of SSI.²³ The authors acknowledged that they did not differentiate between superficial and deep infections, and several studies have found that NPT does not improve outcomes of deep infections, only superficial ones. Additionally, it's possible that their expected reduction in SSI by 20% was an overestimation and a smaller difference could have still been clinically meaningful.

While ERAS does not suggest the use of NPWT, in 2022, 15 colorectal surgeons in a modified Delphi process achieved consensus on intraoperative technical/surgical aspects of SSI prevention. The panel

Table II Comparison of dressings for surgical site infection prophylaxis, and the current guideline consensus for use						
Surgical Site Wound Infection Prophylaxis Options						
	NPWT	Silver-containing Dressing	Mupirocin Dressing	Gentamycin-Collagen Sponge	Vitamin E/Silicon Dressing	
Image			Muptrocin Ointment LP C	annor an I		
Description	Application of sub- atmospheric pressure to aid in reduction of inflammatory exudate and promote granulation tissue.	A diverse range of dressings which utilize the ionization of silver, which inhibits bacterial replication.	Dressing which incorporates mupirocin, which impedes protein and RNA synthesis, leading to bacterial death.	Implantable topical antibiotic agent which disrupts mRNA translation, and thus, protein formation. Par- ticularly useful against certain gram-negative pathogens.	Vitamin E modulation of neutrophil recruitment to damaged tissue.	
Indications	Complex wounds with high risk of non-healing.	Few to no formal recommendations specific to colorectal surgeries.	Few to no formal recommendations specific to colorectal surgeries.	Demonstrated use in contaminated sites or wounds with a high-risk infection.	Few to no formal recommendations specific to colorectal surgeries.	
Current Consensus	Not ERAS suggested. Recent studies propose efficiency and cost-effectiveness.	Mixed results regard- ing the full extent of SSI reduction. Potential for SSI prophylaxis has been demonstrated.	Varying reports of SSI reduction, or lack of. Concern for use due to growing mupirocin resistance and inability to cover gram negative pathogens.	Possible mechanism of the sponge harboring bacteria and increasing SSI, though studies have shown potential for SSI prophylaxis.	Definitive conclusions are scarce among the literature. Resistance of anaerobic bacteria has been shown.	

supported the use of closed-incision negative pressure wound therapy in high-risk, contaminated wounds. The American College of Surgeons and World Society of Emergency Surgery have also noted potential benefits of SSI reduction, specifically over stapled skin in colorectal cases or high-risk patients.^{24, 25}

A randomized control trial in 2019 assessed the impact of prophylactic NPWT on the incidence of SSI in a cohort of high-risk patients undergoing open colorectal surgery. Patients were classified as high risk if they had one or more of the following factors: pre- or postoperative stoma, diabetes mellitus, obesity, preoperative steroids, immunosuppressant use, and/or a contaminated/dirty wound. It concluded a significant reduction in SSI in the NPWT group and half as frequent readmissions in NPWT patients compared with the control group. Mortality, postoperative length of stay, and other wound complications were similar between the groups.²¹

With early mobilization considered an important component of ERAS, the creation of portable NPWT devices has led to improved usage as a dressing option with improved patient-friendly management and mobility. It does not need a canister to collect fluids (canister-free), which are to be absorbed by specifically designed gauze. Once activated, batteries work for seven days, and there is no need for a dressing change-unless the gauze becomes too wet. The NPsealTM (Guard Medical Inc, Miami, Florida) dressing is a specific example of a portable NPWT device.²⁶ In addition to eliminating tubes and canisters, NPsealTM has eliminated the need for an electronic or batterybased energy source. Negative pressure is generated by pinching a small tube integrated into the dressing creating pressures from -75mmHg to -125mmHg and is effective for up to eight hours. The simple design is user-friendly and more cost-effective than traditional NPWT devices.

A study analyzing the impact of prophylactic NPWT compared to sterile gauze in high-risk colorectal wounds was published in 2022. It showed promising results with a significant decrease in both SSI and seroma with NPWT in high-risk patients, with 8.3% of patients in the intervention group developing an SSI versus 30.8% in the control.²⁷ A systematic review of randomized clinical trials on prophylactic negative pressure wound therapy for closed laparotomy wounds was completed in 2020, and it concluded a significant overall reduction in SSI with the use of prophylactic NPWT.

Negative pressure wound therapy application is met with hesitancy because of its higher cost compared to traditional dressings. An analysis was performed in 2022 of the cost-effectiveness of NPWT to prevent SSI after elective colorectal surgery. The study found when the patient's risk of SSIs was greater than 3.2%, negative pressure wound therapy was a cost-effective strategy.28 As previously mentioned, the rate of SSI in colorectal surgery surpasses this threshold, suggesting the cost-effectiveness of NPWT as infection prophylaxis. Innovations in the development of lower cost NPWT are occurring to mitigate this barrier to use.

Silver-containing dressing

The topical antimicrobial agent silver has been used for hundreds of years in wound care.²⁹ In recent years, a wide range of wound dressings that contain elemental silver or a silver-releasing compound have been developed. Topical antiseptics, such as silver, differ from antibiotics in that they have multiple sites of antimicrobial action on target cells and therefore confer a low risk of bacterial resistance.³⁰ Silver, as a metal, is relatively inert and poorly absorbed by cells. When it is exposed to a wound or other body fluids, it ionizes and becomes highly reactive to proteins and cell membranes.²⁹ It has been shown to interact with structural proteins and DNA, inhibiting bacterial replication and causing fatal structural changes within bacterial cell walls.³¹

Evidence surrounding the use of silver-containing dressings as infection prophylaxis in colorectal surgery is limited. A major indication for silver dressing in acute or chronic wounds is to reduce bioburden in wounds that are infected or are being prevented from healing by microorganisms, and/or act as an antimicrobial barrier in wounds at high risk of infection or re-infection. To date, there are no formal recommendations on the use of silver dressings to decrease SSI in colorectal surgeries.

Krieger et al. published the first prospective, randomized, controlled trial analyzing the silver nylon dressing in patients undergoing colorectal surgery. The total incidence of SSI in the silver nylon group was 13%, which was significantly lower than the 33% in the control group (p=0.01).³² This was followed by a 2012 trial by Bifi et al. that compared AQUACEL[®] Ag Hydrofiber[®] (Convatec Group plc, Reading, United Kingdom; silver-containing dressing) to conventional dressings following elective colorectal cancer surgery. The overall rate of SSI was lower in the experimental group, but the observed difference was not statistically significant: there were nine (15.5%) SSIs of any grade in the experimental group and 11 (20.4%) in controls (p=0.623). The results of this randomized trial conflict with those initially reported by the group, summarizing the data of a pilot study carried out in 100 patients consecutively receiving an AQUACEL[®] Ag Hydrofiber[®] dressing after elective colorectal cancer surgery. They observed an overall SSI rate of 4%, which is much less than the 15.5% detected in this randomized trial. The overall higher rate of SSI is similar to the pre-study rates at the participating hospitals and those reported in other studies³³ and is still lower than the rates reported in trials that used the CDC definition of infection and had adequate follow up.^{3,34}

One meta-analysis of RCTs found that ionized silver dressings, applied to a closed wound, were associated with fewer SSIs compared with placebo after CRS (RR=0.55; 95% CI 0.35–0.85).³⁵ A more recent 2022 pilot study of 32 patients evaluated the effect of a silver Hydrofiber[®] dressing on the development of SSIs after ostomy closure.³⁶ The results were significant for no wound infection within 30 days after the operation in the study group, which was statistically significant compared to the four SSIs in the control group (p=0.043). This was the first study in the literature to show that the development of SSIs can be prevented with the use of silver dressings in ostomy closures; however, small sample size was a major limitation.

The use of silver dressings as SSI prophylaxis has yet to be fully defined and evaluated. Current literature suggests potential benefits of their use for surgical sites following colorectal surgery and other clean-contaminated/contaminated operations.

Mupirocin dressings

The antibiotic mupirocin (pseudomonic acid A) is produced by the bacterium *Pseudomonas fluorescens*. Mupirocin calcium ointment was clinically introduced in the late 1980s with the elimination of nasal staphylococci, including methicillin-resistant *S. aureus* (MRSA), the major therapeutic indication. It is often used for the treatment of MRSA, which largely causes nosocomial bloodstream infections and is a major pathogen involved in wound infections.³⁷ Mupirocin is a competitive inhibitor of bacterial isoleucyl-tRNA synthetase and is active against most 'Grampositive' and some 'Gram-negative' bacilli. Mupirocin-mediated inhibition of isoleucyl-tRNA synthetase impedes protein and RNA synthesis, ultimately lead-

ing to bacterial death. In 2016, ACS stated that mupirocin topical antibiotic application can decrease SSI compared with a standard dressing.²⁴ This followed findings in a study that showed that a mupirocin ointment dressing achieved better results for the prevention of SSI than ionic silver-containing dressing or standard dressings in patients undergoing elective open-colorectal surgery. However, a 2019 RCT of mupirocin dressings found no difference in SSI compared with standard gauze when applied to wounds closed with staples or sutures in elective colorectal surgery (2% vs. 3%; p=0.56).³⁸ In both studies, a layer of mupirocin was spread over the surgical site and covered with a generic postoperative dressing, rather than a dressing embedded with the antibiotic. This application differs from the other prophylactic dressing types discussed in this paper.

Preventative use of mupirocin-dressings in high-risk patients is inconclusive in the setting of SSI. Mupirocin resistance is a growing concern due to uncontrolled use, making it a less than ideal option for prophylactic measures. Additionally, it does not cover gram negative pathogens due to its inability to target the membrane barriers, which has led to additional antibacterial mechanistic studies.³⁹ In a 2020 multicenter prospective study, Escherichia coli and Klebsiella pneumoniae, both gram-negative pathogens were the most frequently isolated microorganisms from SSI after colorectal surgery.⁴⁰ These shortcomings in antibacterial coverage make mupirocin-dressings a less ideal candidate compared to other alternatives. Further exploration of the use of mupirocin-dressings for SSI prophylaxis is warranted.

Gentamicin-collagen sponge

Local administration of gentamicincollagen sponges (GCS) has been shown to decrease the wound infection rate significantly after procedures in contaminated sites or surgeries with a high risk of infection. Gentamicin is an aminoglycoside antibiotic used in the treatment of several gram-negative infections, including Escherichia coli, Klebsiella pneumoniae, Serratia spp., Enterobacter spp., and Pseudomonas aeruginosa. Gentamicin passes through the gram-negative membrane in an oxygen-dependent active transport. Once in the cytoplasm, gentamicin selectively binds 16s rRNA at the 30s ribosomal subunit, disturbing mRNA translation and leading to the formation of truncated or non-functional proteins. The gentamicin-collagen sponge, an implantable topical antibiotic agent, is approved for surgical implantation in 54 countries. The sponges received approval in 1985 in Germany, and since 1985, more than one million patients have been treated with GCSs across a range of clinical indications.

Several studies suggest that the sponge may be effective in the prevention and treatment of infections after procedures in contaminated sites or those that are at high risk of infection.^{41, 42} In a 2015 RCT, the local administration of GCS showed no significant benefit regarding wound infection after standardized laparoscopic colorectal resections. However, there was a trend toward reduced SSI in the GCS group (8.2 % in the GCS group and 11.3% in the control).⁴³ One notable limitation was the lower incidence of SSI in the control group. Researchers theorized that this could be due to the overall lower incidence of SSI with laparoscopic techniques.

GCSs have various shortcomings. Notably, one randomized trial showed that the insertion of GCS after colorectal surgery led to a higher incidence of SSI.⁴⁴ The investigators hypothesized explanations for these unexpected findings including that they found what appeared to be a transient early benefit of the sponge with a successive reversal in that effect. This benefit reversal may be consistent with the failure of the sponge to provide a sustained local level of gentamicin. A sponge with depleted antibiotic levels could harbor bacteria, thereby increasing the risk of infection.

Vitamin E and silicon dressings

Vitamin E is an immunomodulator that reduces edema and moderates the increase of cyclo-oxygenase-2, an enzyme that catalyzes the synthesis of prostaglandin E2, involved in the local inflammatory response to stimuli.⁴⁵ In addition, it has been shown to modulate neutrophil recruitment to damaged tissue.⁴⁶ We were able to find one study to date-published in 2019, by Ruiz-Tovar—comparing the use of vitamin E/silicon (E-Sil) dressings to conventional dressings in colorectal surgery. This study found that the white blood cell (WBC) count and C-reactive protein (CRP) level were significantly higher in the conventional dressing group. The incisional SSI rate was greater in these patients inferring that the higher WBC count and CRP level could be attributed to an incipient infection.⁴⁷ The only micro-organisms causing incisional SSI in the E-Sil group were Bac*teroides fragilis*, with complete reduction in infections due to Escherichia coli, Streptococcus spp., and Klebsiella spp. Compared to the conventional dressing group. This may be explained by the fact that vitamin E acts as a cofactor in the hydrogenization of unsaturated fatty acids, induced by anaerobic micro-organisms alone, leading to local reduction of these fatty acids, including omega-3 fatty acids. Omega-3 fatty acids demonstrate a bacteriostatic and bactericidal mechanism which may be lost with hydrogenation.48,49 This may explain the resistance of anaerobic bacteria to the bactericidal and immunomodulatory effect of vitamin E. Additional research is needed to make more definitive conclusions on the efficacy of vitamin E dressings in reducing SSI following colorectal surgery.

CONCLUSION

Many patient factors exist that lead to poor wound healing and poor wound perfusion but have yet to be successfully corrected for or optimized. The bacterial load and virulence of specific bacteria colonized in individual patients have yet to be established in the perioperative timeframe, which may influence dressing choice postoperatively. Additionally, surgical techniques used during colorectal surgery are not currently standardized leading to high variability in clinical care depending on surgeon preferences.

The evolving wound care devices researched in this article show a small step towards identifying and implementing best practice in caring for postoperative wounds following colorectal procedures. There is a need for highquality studies comparing various strategies of postoperative wound management and this is certainly an area for additional research. **SII**

AUTHORS' DISCLOSURES

The authors have no conflicts of interest to disclose.

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