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The Efficacy of Negative Pressure Wound Therapy and Antibiotic Beads in Lower Extremity Salvage

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ABSTRACT

Background: Antibiotic beads and negative pressure wound therapy (NPWT) represent two methods of wound management used during staged debridement in the post-trauma limb salvage pathway. The efficacy of NPWT and antibiotic beads in preventing infection remains unclear.

Methods: This study is a retrospective review of patients with traumatic lower extremity open fractures who received NPWT and/or antibiotic beads before soft tissue reconstruction at an urban level 1 trauma center between August 2007 and December 2015. Patients with wound infections before application of NPWT and/or antibiotic beads were excluded.

Results: In 73 lower extremities requiring soft tissue coverage, 46 received antibiotic beads and 48 received NPWT. Overall infection rate was 15.1%. Use of antibiotic beads was associated with a decreased risk of infection (6.4% *versus* 30.7%; $P = 0.01$). Use of NPWT was associated with an increased risk of one or more complications (45.7% *versus* 4.2%; $P = 0.001$). The development of infection was associated with a greater period of time between application of antibiotic beads (22 ± 13 *versus* 12 ± 6 d, $P = 0.01$) or NPWT (23 ± 15 *versus* 10 ± 11 d, $P = 0.004$) and soft tissue coverage. Overall limb salvage rate was 95.9%; secondary amputation was associated with development of infection ($P = 0.001$) but not with use of NPWT or antibiotic beads.

Conclusions: Antibiotic beads may prevent infections in patients awaiting soft tissue coverage of wounds. NPWT may contribute to a greater rate of complication. Limb salvage was successful in most cases regardless of method of wound management.

Introduction

With recent advances in microsurgery, lower extremity salvage via placement of muscle and fasciocutaneous flaps has become the standard of care in patients with severe traumatic lower extremity soft tissue defects. Despite high salvage rates, these patients often face major complications. The Lower Extremity Assessment Project, an extensive multicenter prospective study designed to understand and to improve limb salvage outcomes, identified infection as one of the most commonly reported wound complications, affecting approximately one in four trauma patients awaiting lower

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extremity reconstruction.[1] Open fractures in the lower extremity are more likely to develop deep infections than open fractures in other locations.[2] Reported infection rates after open tibial fractures range from 11% to 50% depending on the Gustilo grade of the injury.[3-6] These infections compromise patient functional recovery by preventing bony union after orthopedic interventions and may lead to salvage failure and the need for late amputation.[7] Consequently, it is crucial to take measures to prevent these events.

Antibiotic bead pouches have traditionally been the standard of care for staged debridement before definitive soft tissue reconstruction during attempted limb salvage. A major advantage of using antibiotic beads is the ability to deliver a high antibiotic concentration locally, preventing bacterial growth at the wound site while limiting systemic side effects.[8] In addition, beads allow antibiotics to reach wounds with compromised vascularity that cannot be accessed by systemic administration.[9] Several studies have validated the use of antibiotic beads as deep infection prophylaxis in open fractures. Their use is associated with the prevention of osteomyelitis, a reduction in infection rates, and decreased bacterial counts.[8,10-13]

One alternative to antibiotic beads for wound management in open tibial fractures is negative pressure wound therapy (NPWT). In addition to increasing blood flow to the wound and removing exudative fluid rich in cytokines, NPWT acts as an occlusive dressing to physically protect the wound from the entry of nosocomial contaminants.[14] NPWT is often used as temporary coverage and may allow for delayed coverage of up to 7 d before rates of skeletal and flap complications increase.[15,16] However, the efficacy of NPWT in infection prevention is controversial. The WOLFF trial, a large multicenter randomized prospective study, found no significant difference between the rate of deep surgical site infections among adults using NPWT and standard dressings after open fractures of the lower limb.[17]

There is limited literature comparing NPWT with the alternative of antibiotic beads. Warner *et al.* (2010) studied these two methods of local wound management in a military blast wound population, most with traumatic amputations with a large zone of injury and a high degree of contamination. They found that patients receiving NPWT had more methicillin-resistant *Staphylococcus aureus* (MRSA) infections, more wound care problems requiring unanticipated returns to the operating room for irrigation, and debridement after primary closure, and more surgeries overall before definitive wound closure than those receiving antibiotic beads.[18] Our primary aim is to establish the efficacy of NPWT and antibiotic beads at preventing infections and complications in a civilian population with open lower extremity fractures necessitating definitive flap coverage. Our secondary aim is to quantify the relationship of infection to operative characteristics and limb salvage. Based on existing literature, we hypothesize that use of antibiotic beads will be associated with decreased rate of infection and consequently decreased rate of complications that NPWT will be associated with no difference in infection or complication rate. In addition, we hypothesize that development of infection will be associated with delayed definitive soft tissue coverage, a greater number of operations, and lower rates of limb salvage.

Methods

Study design

A retrospective chart review of a prospectively maintained database of free and local tissue transfers to the lower extremities was performed on patients presenting to Los Angeles County Hospital from August 2007 through December 2015. Approval with a waiver of informed consent was received from the institutional review board at the Keck School of Medicine of the University of Southern California. No funding was utilized for this study. Inclusion criteria included attempted lower extremity salvage of an open fracture resulting from a traumatic mechanism of injury with use of NPWT and/or antibiotic beads during the course of hospitalization. Exclusion criteria included the development of infection before the application of antibiotic beads or NPWT. In patients receiving both antibiotic beads and NPWT, patients who developed infection before application of the second treatment were excluded; the purpose of this approach was to prevent biasing the data with patients who developed infection while using NPWT and were consequently switched to an antibiotic bead regimen in an attempt to clear the infection. The control group for each wound management method used the patient group that passed inclusion/exclusion criteria and did not receive the management method of interest.

Modalities of wound management

Use of antibiotic beads was defined by exposure to high-dose antibiotic-loaded cement during the period between injury and definitive wound closure, with or without the concurrent or independent use of NPWT. Use of NPWT was defined as exposure to subatmospheric pressures *in situ*, with or without the concurrent or independent use of antibiotic beads. At our institution, NPWT is delivered using the vacuum-assisted closure therapy system (KCI Inc, San Antonio, TX) applied in the operating room under sterile conditions and changed every three to 5 d at bedside or under sterile conditions. To prepare the dressing for NPWT, a polyurethane sponge is placed into the wound and covered by a nonadherent dressing film to create an air tight seal. The SensaTRAC pad is applied over an opening in the dressing and suction is applied continuously at a pressure of 125 mmHg. Antibiotic beads are formed from 1 g vancomycin and 2.4 g tobramycin per packet of Simplex P Bone Cement (Stryker, Mahwah, NJ) polymethyl methacrylate powder. The antibiotic cement is formed into pea-sized spheres on a string of suture material for ease of removal. The beads are placed at the injury site after irrigation and debridement of the wound and covered with gauze and an adherent occlusive dressing (Ioban, 3M, St Paul, MN). Patients in the study additionally received systemic prophylactic antibiotics based on their injuries and comorbidities, typically cefazolin and gentamicin. All patients diagnosed with lower extremity infection were treated with therapeutic antibiotics and/or debridement and soft tissue coverage per the accepted standard of care. Systemic antibiotics were selected on the basis of empirically based guidelines and local resistance profiles.

Table 1 – Patient demographics and mechanism of injury.

	No beads (NPWT only)	No NPWT (beads only)	Use of beads	Use of NPWT	Total	P value; beads *versus* no beads	P value; NPWT *versus* no NPWT	P value; beads only *versus* NPWT only
n (patients)	26 (36.1%)	24 (33.3%)	46 (63.9%)	48 (66.7%)	72			
Mean age	41 ± 17	40 ± 20	37 ± 17	38 ± 16	39 ± 17	0.34	0.65	0.85
Males	23 (88.5%)	23 (95.8%)	39 (84.8%)	39 (81.3%)	62 (86.1%)	0.74	0.15	0.61
Smoking	5 (19.2%)	10 (41.7%)	17 (37.0%)	12 (25.0%)	22 (30.6%)	0.19	0.18	0.12
Hypertension	2 (7.7%)	5 (20.8%)	6 (13.0%)	3 (6.3%)	8 (11.1%)	0.70	0.11	0.24
Diabetes	5 (19.2%)	3 (12.5%)	6 (13.0%)	8 (16.7%)	11 (15.3%)	0.51	0.74	0.70
Immunosuppressed	2 (7.7%)	1 (4.2%)	1 (2.2%)	2 (4.2%)	3 (4.2%)	0.29	1.00	1.00
ASA class								
Class 1	14 (53.8%)	16 (66.7%)	33 (71.7%)	31 (64.6%)	47 (65.3%)	0.20	1.00	0.40
Class 2	11 (42.3%)	8 (33.3%)	12 (26.1%)	15 (31.3%)	23 (31.9%)	0.19	1.00	0.57
Class 3	1 (3.8%)	0 (0.0%)	1 (2.2%)	2 (4.2%)	2 (2.8%)	1.00	0.55	1.00
Mechanism of injury								
Auto *versus* pedestrian	10 (38.5%)	7 (29.2%)	14 (30.4%)	17 (35.4%)	24 (33.3%)	0.60	0.79	0.56
Motor vehicle accidents	5 (19.2%)	6 (25.0%)	8 (17.4%)	7 (14.6%)	13 (18.1%)	1.00	0.34	0.74
Motorcycle collisions	3 (11.5%)	3 (12.5%)	12 (26.1%)	12 (25.0%)	15 (20.8%)	0.23	0.36	1.00
Fall	5 (19.2%)	2 (8.3%)	4 (8.7%)	7 (14.6%)	9 (12.5%)	0.27	0.71	0.42
Gunshot wound	3 (11.5%)	2 (8.3%)	4 (8.7%)	5 (10.4%)	7 (9.7%)	0.70	1.00	1.00
Crush	0 (0.0%)	2 (8.3%)	2 (4.3%)	0 (0%)	2 (2.8%)	0.53	0.11	0.23
Blast	0 (0.0%)	2 (8.3%)	2 (4.3%)	0 (0%)	2 (2.8%)	0.53	0.11	0.23

Data collection and outcomes

Patient characteristics such as age, gender, anthropometrics, mechanism of injury, comorbidities, medications, and immune status were collected from electronic medical records. Immunosuppression was defined as chronic use of an immunosuppressant medication, inherited immune condition, or meeting diagnostic criteria for stage three human immunodeficiency virus infection (i.e., acquired immune deficiency syndrome) as defined by the Centers for Disease Control and Prevention.[19] Chronological data included date of injury, date of NPWT/bead application, and date of flap surgery. Presence of infection was determined on the basis of provider notes, laboratory microbiology results of wound and bone cultures, and radiology findings in cases of osteomyelitis. Delayed and late flap coverage were defined according to Godina's classification as occurring at 72 h to 90 d, and 90 or more days after injury, respectively.[20] The primary outcome of this study was to compare the incidence rate of infection and complications. Lower extremity infection was defined as a soft tissue infection, hardware infection, or osteomyelitis of the lower extremity to which soft tissue coverage was applied; only wound infections developing between antibiotic beads and/or NPWT placement and within 6 wk after definitive soft tissue coverage were considered. Flap complications included flap necrosis, fat necrosis, flap failure, and wound dehiscence. Flap failure was defined as complete flap necrosis requiring amputation or necessitating debridement and placement of a new flap.

Statistical analysis

Continuous variables were compared using the two-tailed unpaired *t*-test. Discrete variables were assessed for significant differences with a two-tailed Fisher's exact test. Odds ratios and 95% confidence intervals were calculated for groups showing a significant difference, which was defined as $P \leq 0.05$.

Results

Demographics and comorbidities

Of the 190 patients identified as receiving free and local tissue transfers to the lower extremities, 72 patients passed the inclusion and exclusion criteria. The mean age was 39 ± 17 y (range: 16 to 84 y), and the majority were male (86.1%). Eleven patients (15.3%) had diabetes and 22 (30.6%) smoked. All patients had an American Society of Anesthesiologist class of III or less. Most patients had a blunt mechanism of injury (90.3%) with motor vehicle *versus* pedestrian (33.3%), motorcycle collisions (20.8%), and motor vehicle *versus* vehicle or object (18.1%) being most common. There was no significant difference in age, smoking status, diabetes, hypertension, immune status, American Society of Anesthesiologist class, or mechanism of injury between patients who received NPWT or antibiotic beads and those who did not receive the respective management (Table 1).

A total of 73 lower extremities in 72 patients underwent attempted limb salvage. In addition to cefazolin and gentamicin, 15.1% of patients received systemic antibiotics including Levaquin, cefepime, ciprofloxacin, vancomycin, and Zosyn before flap coverage or to recipient site infection for comorbid conditions; there was no significant difference in use of these systemic antibiotics and application of NPWT ($P = 0.74$) or of antibiotic beads ($P = 0.51$). Most extremities had a tibia or fibula fracture (72, 98.6%), with many having both fractures in conjunction (47, 64.4%). Extremities with either ankle or foot fractures were less common (27, 37.0%). There was no association between the bones fractured and the use of NPWT or antibiotic beads. The most common fracture classification was Gustilo IIIB (41, 56.2%). Patients were significantly more likely to receive NPWT only (no beads) in the setting of Gustilo II (*versus* any use of beads, $P = 0.04$; *versus* beads only, $P = 0.04$) fractures and less likely to receive NPWT only in the setting of Gustilo IIIB (*versus* any use of beads, $P = 0.03$; *versus* beads only, $P = 0.05$) fractures (Table 2).

Perioperative information

Seventy-six lower limb flaps were placed on 73 extremities. Of these extremities, 26 (35.6%) received only NPWT, 24 (32.9%) only antibiotic beads, and 23 (31.5%) both antibiotic beads and NPWT. Fifty flaps were placed over soft tissue defects which had received treatment with antibiotic beads (beads only or NPWT/beads), 52 flaps over NPWT (NPWT only or NPWT/beads), 26 flaps over no beads (NPWT only), and 24 flaps over no NPWT (antibiotic beads only). Patients who did not receive antibiotic beads were more likely to receive a gracilis flap ($P = 0.04$); there were no other significant differences in flap types between groups (Table 3).

Outcomes

There was an equivalent risk of eschar formation, flap necrosis, fat necrosis, flap revision, flap dehiscence, and secondary amputation regardless of NPWT or antibiotic bead utilization. Overall infection rate was 15.1%; patients with and without exposure to antibiotic bead therapy had a 6.4% and 30.7% rate of wound infection, respectively. Use of antibiotic beads was associated with a significantly lower rate of wound infections (OR, 6.5; CI, 1.6-27.4; $P = 0.01$). This finding was independent of whether NPWT was used (beads only *versus* NPWT only; OR, 10.2; CI, 1.2-89.4; $P = 0.02$). There was no significant association between use of NPWT and infection rate ($P = 0.09$). Rates of MRSA infection were 2.7% overall; there was no significant association between antibiotic bead or NPWT use and development of an MRSA infection. Use of NPWT was associated with a significantly increased rate of complications (OR, 17.3; CI, 2.2-138.2, $P < 0.001$); this finding was independent of whether antibiotic beads were used (NPWT only *versus* beads only; OR, 14.4; CI, 1.7-123.7; $P = 0.01$). Neither use of NPWT ($P = 0.26$) nor antibiotic beads ($P = 0.26$) was associated with postcoverage return to the operating room for irrigation and debridement. An overall limb salvage rate of 95.9% was achieved (Table 4).

Comparing patients with Gustilo I or II fractures to those with Gustilo IIIB or IIC fractures found that wound severity

Table 2 – Injury characteristics.

	No beads (NPWT only)	No NPWT (beads only)	Use of beads	Use of NPWT	Total	P value; beads *versus* no beads	P value; NPWT *versus* No NPWT	P value; beads only *versus* NPWT only
n (Extremities)	26 (35.6%)	24 (32.9%)	47 (64.4%)	49 (67.1%)	73			
Wound area (cm^2)	103 ± 103	144 ± 265	155 ± 231	132 ± 158	116 ± 172	0.28	0.81	0.48
Systemic antibiotics[†]	5 (19.2%)	3 (12.5%)	6 (12.8%)	8 (16.3%)	11 (15.1%)	0.51	0.74	0.70
Fracture severity								
Gustilo I	1 (3.8%)	1 (4.2%)	1 (2.1%)	1 (2.1%)	2 (2.7%)	1.00	1.00	1.00
Gustilo II	12 (46.2%)	4 (16.7%)	13 (27.7%)	21 (42.9%)	25 (34.2%)	0.13	0.04*	0.04*
Gustilo IIIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1.00	1.00	1.00
Gustilo IIIB	12 (46.2%)	18 (75.0%)	29 (61.7%)	23 (46.9%)	41 (56.2%)	0.23	0.03*	0.05*
Gustilo IIIC	1 (3.8%)	1 (4.2%)	4 (8.5%)	4 (8.2%)	5 (6.8%)	0.65	1.00	1.00
Location of fracture								
Tibia	23 (88.5%)	24 (100.0%)	46 (97.9%)	45 (91.8%)	69 (94.5%)	0.13	0.30	0.24
Fibula	16 (61.5%)	19 (79.2%)	33 (70.2%)	30 (61.2%)	49 (67.1%)	0.60	0.19	0.22
Ankle	6 (23.1%)	4 (16.7%)	8 (17.0%)	10 (20.4%)	14 (19.2%)	0.55	1.00	0.73
Foot	7 (26.9%)	4 (16.7%)	10 (21.3%)	13 (26.5%)	17 (23.3%)	0.58	0.40	0.50

* $P \leq 0.05$.
† Excludes cefazolin and gentamicin, which all patients received. Also excludes systemic antibiotics started after recipient site infection.

Table 3 – Flap characteristics.

	No beads (NPWT only)	No NPWT (beads only)	Use of beads	Use of NPWT	Total	P value; beads *versus* no beads	P value; NPWT *versus* no NPWT	P value; beads only *versus* NPWT only
Total flaps	26 (34.2%)	24 (31.6%)	50 (65.8%)	52 (68.4%)	76			
Local flap	18 (69.2%)	13 (54.2%)	25 (50.0%)	30 (57.7%)	43 (56.6%)	0.14	0.81	0.38
Gastrocnemius	7 (26.9%)	2 (8.3%)	9 (18.0%)	14 (26.9%)	16 (21.1%)	0.39	0.08	0.14
Soleus	10 (38.5%)	10 (41.7%)	14 (28.0%)	14 (26.9%)	24 (31.6%)	0.44	0.29	1.00
Other	1 (3.8%)	1 (4.2%)	2 (4.0%)	2 (3.8%)	3 (3.9%)	1.00	1.00	1.00
Free flap	8 (30.8%)	11 (45.8%)	25 (50.0%)	22 (42.3%)	33 (43.4%)	0.14	0.81	0.38
Rectus	0 (0.0%)	4 (16.7%)	7 (14.0%)	3 (5.8%)	7 (9.2%)	0.09	0.20	0.05
Latissimus	2 (7.7%)	3 (12.5%)	9 (18.0%)	8 (15.4%)	11 (14.5%)	0.31	1.00	0.66
Anterolateral thigh fasciocutaneous	3 (11.5%)	3 (12.5%)	7 (14.0%)	7 (13.5%)	10 (13.2%)	1.00	1.00	1.00
Gracilis	3 (11.5%)	0 (0.0%)	0 (0.0%)	3 (5.8%)	3 (3.9%)	0.04*	0.55	0.24
Other	0 (0.0%)	1 (4.2%)	2 (4.0%)	1 (1.9%)	2 (2.6%)	0.54	0.53	0.49

* $P \leq 0.05$.

Table 4 – Injury and surgical complications.

	No beads (NPWT only)	No NPWT (beads only)	Use of beads	Use of NPWT	Total	P value; beads *versus* no beads	P value; NPWT *versus* no NPWT	P value; beads only *versus* NPWT only
n (extremities)	26	24	47	46	73			
Overall complication rate	10 (38.5%)	1 (4.2%)	12 (25.5%)	21 (45.7%)	22 (30.1%)	0.29	0.001*	0.01*
Postcoverage return to the OR for debridement	5 (19.2%)	1 (4.2%)	4 (8.5%)	8 (17.4%)	9 (12.3%)	0.26	0.26	0.19
Infection	8 (30.7%)	1 (4.2%)	3 (6.4%)	10 (21.7%)	11 (15.1%)	0.01*	0.09	0.02*
MRSA	1 (3.8%)	1 (4.2%)	1 (2.1%)	1 (2.2%)	2 (2.7%)	0.49	0.18	1.00
Eschar	2 (7.7%)	1 (4.2%)	6 (12.8%)	7 (15.2%)	8 (11.0%)	0.70	0.25	1.00
Fat necrosis	0 (0.0%)	1 (4.2%)	2 (4.3%)	1 (2.2%)	2 (2.7%)	0.54	1.00	0.48
Flap revision	1 (3.8%)	0 (0.0%)	3 (6.4%)	4 (8.7%)	3 (4.1%)	1.00	0.30	1.00
Wound dehiscence	3 (11.5%)	0 (0.0%)	1 (2.1%)	4 (8.7%)	4 (5.5%)	0.13	0.30	0.24
Complete flap necrosis	2 (7.7%)	0 (0.0%)	0 (0.0%)	2 (4.3%)	2 (2.7%)	0.12	1.00	0.49
Amputation	2 (7.7%)	0 (0.0%)	1 (2.1%)	3 (6.5%)	3 (4.1%)	0.13	0.55	0.49

* $P \leq 0.05$.

showed no significant interaction with antibiotic bead or NPWT use in rates of infection ($P = 1.00$; $P = 0.74$) or complication ($P = 0.42$; $P = 0.75$), respectively. The decreased rate of wound infection with use of antibiotic beads persisted in subgroup analysis of Gustilo IIIB/IIIC fractures (OR, 6.9; CI, 1.1-43.9; $P = 0.05$; Table 5).

There was no correlation in time from injury to placement of NPWT ($P = 0.07$) or antibiotic beads ($P = 0.76$) and risk of infection. All patients underwent delayed or late flap coverage, with the earliest flap placement occurring 6 d from injury and the latest at 99 d. There was no significant difference in time between changes of the NPWT vacuum dressing in patient who developed an infection and patients who did not develop infection (4 ± 0.8 d, 3.5 ± 1.0 d, $P = 0.13$). Patients who developed a wound infection had a significantly greater number of days from initiation of NPWT to definitive soft tissue coverage (23 ± 15 *versus* 10 ± 11 d, $P < 0.01$) or initiation of antibiotic beads to definitive soft tissue coverage (22 ± 13 *versus* 12 ± 6 d, $P < 0.01$) than patients who did not develop an infection. The time from injury to definitive soft tissue coverage was significantly greater in patients who developed infections (29 ± 15 d) than in patients without infections (18 ± 15 d, $P = 0.03$). Development of infection correlated with a greater number of operations (4.9 ± 2.0 *versus* 3.8 ± 1.4, $P = 0.05$) between the time of injury and flap placement, as well as increased risk of secondary amputation ($P = 0.003$) (Table 6). All amputations were to infected limbs.

Discussion

Antibiotic beads and NPWT are widely used in the management of post-trauma lower extremity wounds pending flap coverage. We aimed to determine the effect of these wound management modalities on patient outcomes. The rates of wound infection in this study (15.1% overall) were consistent with rates reported in the literature for lower extremity fractures.[3-6] The use of antibiotic beads was associated with a significantly decreased incidence of infection ($P < 0.01$). The use of NPWT was associated with a significant increase in overall complication rate ($P < 0.001$), without a significant difference in infection rate ($P = 0.09$).

The results of this study support prior clinical research suggesting that use of antibiotic beads is effective in preventing infection in the setting of orthopedic trauma.[8,10,11] The finding that beads were associated with lower rates of infection may be due to the superior prophylactic ability of bactericidal antibiotics *versus* the more indirect effects of NPWT.[21,22] Alternatively, differences in infection rates may be due to differences in the maintenance of beads *versus* NPWT. The occlusive dressing of the antibiotic bead dressing and the NPWT apparatus act as barriers between the wound and the surrounding environment.[23] NPWT is often changed at bedside, and although care is taken to maintain a clean environment, the lack of sterility may contribute to introduction of organisms into the wound. By contrast, antibiotic beads are always exchanged in the operating room, where sterile conditions are consistently maintained while the wound is open to the environment.

Table 5 – Subgroup analysis by Gustilo classification.

	No beads (NPWT only)	No NPWT (beads only)	Use of beads	Use of NPWT	Total	P value; beads *versus* No beads	P value; NPWT *versus* no NPWT	P value; beads only *versus* NPWT only
Gustilo IIIB and IIIC								
n (extremities)	13	19	33	27	46			
Infection	4 (30.8%)	1 (5.3%)	2 (6.1%)	5 (18.5%)	6 (13.0%)	0.05*	0.37	0.13
Complication	3 (23.1%)	1 (5.3%)	5 (15.2%)	7 (25.9%)	8 (17.4%)	0.67	0.11	0.28
Gustilo I and II								
n (extremities)	13	5	14	22	27			
Infection	4 (30.8%)	0 (0.0%)	1 (7.1%)	5 (22.7%)	5 (18.5%)	0.16	0.55	0.28
Complication	3 (23.1%)	0 (0.0%)	4 (28.6%)	7 (31.8%)	7 (25.9%)	1.00	0.28	0.52

* $P \leq 0.05$.

Whereas other studies have found a decrease in wound infection rates with the utilization of NPWT, this study found no such benefit.[24-27] This difference may be attributable to our use of antibiotic beads as the alternative study group, whereas the cited studies used standard gauze dressing as the alternative to NPWT. NPWT pump failure has been shown to contribute to wound complications and higher rates of infection, as the sponge acts as a foreign body and static blood acts as a medium for bacterial growth.[28] Suction failure was not able to be reliably ascertained because of the retrospective nature of this study and could have biased results. Our results support the conclusion of the WOLFF trial that use of NPWT on open fractures of the lower limb may not affect the risk of infection. However, it should be noted that the WOLFF trial achieved a power of 0.9; there is a 10% probability that there is a true association between NPWT use and infection rates which the study fails to identify.[17] Warner *et al.*[18] found that compared with patients receiving antibiotic beads, NPWT was associated with a higher risk of MRSA infection, more returns to the operating room, and more surgeries overall. Our study indicates that antibiotic beads may be effective at preventing infection in civilian patients but did not find a significant correlation in use of NPWT or antibiotic beads and the development of MRSA infection or postoperative return to the operating room for irrigation and debridement. This may be explained by differences in mechanism (majority motor vehicle collision *versus* blast wounds from improvised explosive devices), setting (Los Angeles County Hospital *versus* Afghanistan Combat Support Hospital), and severity (salvageable fractures *versus* traumatic amputations) of injuries between our study group and that of Warner *et al.*

The development of infection may have contributed to prolonged and ultimately unsuccessful attempts at limb salvage. Infection correlated significantly with a delay in flap coverage ($P = 0.03$), a greater number of operations before coverage ($P = 0.05$), and a higher incidence of secondary amputation ($P = 0.003$). The increased number of operations and delay in flap coverage may be attributable to the need for serial irrigation and debridement of necrotic infected tissue to prepare the wound for soft tissue coverage. Our finding of increased incidence of secondary amputation in the setting of infection supported those of Huh *et al.*[7] Given that antibiotics beads were significantly associated with decreased rates of infection, and that all secondary amputations occurred after infection of the recipient site, it is likely that the lack of association between antibiotic beads and amputation was a result of type 2 error due to insufficient power from low rates of secondary amputation (i.e., high rates of successful limb salvage) in the study population. Due to the potential for failed limb salvage in the setting of infection, it is important to consider methods of wound management in planning the reconstructive course.

The broad range of patient demographics and of injury characteristics, as well as the diversity of mechanisms of injury, makes our results broadly applicable to a variety of patients with traumatic lower extremity injuries requiring soft tissue reconstruction. However, this study was subject to several limitations. First, as this was a retrospective review, we cannot definitively determine causality in the relationship between antibiotic bead use and infection rate, NPWT use and

Table 6 – Infection and operative time course.

	Infection	No infection	Total	P-value
N (extremities)	11	62	73	
Secondary amputation	3 (27.3%)	0 (0.0%)	3 (4.1%)	0.003*
Number of operations	4.9 ± 2.0	3.8 ± 1.4	3.9 ± 1.5	0.05*
Days from injury to definitive closure	29 ± 15 (range 9-37)	18 ± 15 (range 6-99)	19 ± 15 (range 6-99)	0.03*
NPWT				
N (extremities)	10	36	46	
Days from injury to NPWT	30 ± 15	19 ± 17	11 ± 17	0.07
Days between NPWT changes	4 ± 0.8	3.5 ± 1.0	3.6 ± 1.0	0.13
Days from initiation of NPWT to definitive closure	23 ± 15	10 ± 11	13 ± 13	0.004*
Antibiotic beads				
N (extremities)	3	44	47	
Days from injury to beads	9 ± 8	11 ± 11	5 ± 9	0.76
Days from initiation of beads to definitive closure	22 ± 13	12 ± 6	13 ± 7	0.01*

*$P \leq 0.05$.

complication rate, or development of infection and delay in closure. In addition, the electronic medical records used in this study may have omitted or contained incomplete information, negatively impacting the veracity of our results. This study only evaluated objective complication rates after NPWT and antibiotic beads and does not account for a number of other factors important for limb salvage process including patient comfort, quality of life, and cost stratification of these two wound coverage modalities. Patients using NPWT may benefit from its ability to promote development of granulation tissue and to bring wound edges together. It is possible that smaller wounds with healthy underlying tissue were able to undergo primary closure or skin grafting rather than flap coverage after the use of NPWT. These patients would not be represented in our study population and would skew the NPWT group to include the patients with wound characteristics that make them less amenable to coverage using lower rungs of the reconstructive ladder. This is supported by the finding that patients who presented with Gustilo II fractures (small defects) were more likely to receive NPWT, and patients with Gustilo IIIB fractures (large defects) were less likely to receive NPWT before flap coverage. However, there was no significant difference in calculated wound area, or in rates of comorbidities known to affect wound healing (i.e., smoking, diabetes) between patients using NPWT and those who did not. Based on these limitations, future prospective studies with larger sample sizes may be necessary to confirm the differences in efficacy between antibiotic beads and NPWT in infection prophylaxis for patients awaiting limb salvage.

Conclusion

In patients awaiting definitive soft tissue coverage of lower extremity traumatic wounds, the use of antibiotic beads may be preferable to NPWT in wound management. Patients using antibiotic beads experienced lower rates of wound infection, whereas in patients utilizing NPWT, increased overall complication rates were found. Antibiotic beads may reduce or prevent infection, although we are unable to confirm that their use prevents amputation in these at-risk limb salvage patients.

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Disclosure

The authors reported no proprietary or commercial interest in any product mentioned or concept discussed in this article.

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