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Efficacy of Power-pulsed Lavage in Lower Extremity Wound Infections: A Prospective Observational Study

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ABSTRACT

Power-pulsed lavage is a common adjunct to surgical wound debridement, although few studies have examined the effect of this technique in lower extremity wounds. Fifty-five consecutively enrolled patients underwent 73 surgical debridements with power-pulsed lavage, and specimens were obtained for Gram stain and culture and sensitivity analyses before and after lavage. A number of risk factors were analyzed in regard to a successful outcome, which was defined as the absence of any organisms observed on the immediate postlavage culture. The incidence of a successful outcome was 69.86%, and debridement plus power-pulsed lavage statistically significantly decreased bacteria between the immediate prelavage and immediate post-lavage specimens, for Gram stain ($P = .0004$) and culture ($P = .005$) analyses. Generalized estimation equations provided fully adjusted effect estimates that revealed a decreased likelihood of observing success if the patient's age was 85 years or older, or if rare or many organisms, or gram-negative rods, were present on the immediate prelavage Gram stain; whereas an increased likelihood of success was observed if the patient's body mass index was indicative of normal weight, and if few bacteria were noted on the immediate prelavage culture specimen. Based on these results, we concluded that power-pulsed lavage can be effective in decreasing the presence of bacteria in lower extremity wounds, and an awareness of the patient characteristics and microbiological factors associated with the persistence of bacteria may be helpful to surgeons treating such wounds.

Lower extremity wounds pose a burden to the health care system in terms of time and money spent, and to patients in terms of morbidity and, in some cases, mortality. Lower extremity wounds are a common problem, and for persons with diabetes mellitus the prevalence of such wounds has been reported to range from 4% to 10% (1). In fact, in a study of data for 419 diabetic men and women aged 40 years or older, from the 1999–2000 National Health and Nutrition Examination Survey, 9.5% (95% confidence interval [CI] 5.5% to 13.4%) displayed peripheral arterial disease (ankle-brachial index < 0.9), 28.5% (95% CI 22.0% to 35.1%) peripheral neuropathy (≥ 1 insensate area based on monofilament testing), and 30.2% (95% CI 22.1% to 38.3%) lower extremity disease (peripheral arterial disease, peripheral neuropathy, and/or a history of a foot ulcer) (2). Still further, the proportion of lower extremity wounds failing to heal following amputation for the treatment of diabetic neuropathic foot ulceration was shown to be 34.01% (3). It should also be noted that infection is generally considered to be the most common cause of delayed healing in surgical wounds, and surgical wound infection may lead to systemic infection and prolonged hospitalization. If the body is unable to contain wound surface microbiological contamination, then wound infection may develop. Leidberg et al (4) showed that a bacterial concentration of more than 100,000 organisms per gram of tissue leads to local tissue destruction and bacterial multiplication, and advised that such a concentration of organisms should be clinically considered an infection because the bacteria tend to multiply and spread from the local site. Similarly, Robson and Heggers (5) noted wound sepsis and failure to heal were clinically apparent in wounds with bacterial counts greater than 100,000 organisms per gram of tissue. Theoretically, contamination disrupts collagen synthesis and alters matrix metalloproteinases (MMPs), leading to anoxia and inhibiting neutrophil and macrophage function. It has also been shown that necrosis in a wound or at its margin disables wound epithelialization and contraction (6–8). It is also known that the presence of necrosis acts as a nidus for infection (8). Once identified, surgical debridement is considered standard of care for grossly contaminated and infected wounds.

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Debridement of wounds was first described in the 18th century by Desault (9), and has since evolved to include a wide range of techniques, chief among them being thorough irrigation. Wound irrigation is typically combined with debridement in order to remove infected and necrotic tissues and debris from the wound surface, and is generally considered to be standard surgical practice. Power-pulsed lavage (PPL) is a method of wound irrigation that uses an electrically powered pump system to deliver a high volume of an irrigation solution under pressure. The pressure produced and volume delivered by a PPL system is generally considered greater than that produced with a standard bulb syringe or small syringe and plunger. A series of studies performed at the US Army Institute of Dental Research, at Walter Reed Medical Center in Bethesda, Maryland, provided results that supported the efficacy of PPL in regard to removal of loose debris and pathogens (10), and disruption of bacterial adherence by means of fluid dynamic forces (11).

Multiple studies have examined the effects of PPL in animal wound models (12–14), in vitro bone models (15, 16), and inanimate bench top objects (17, 18). Moreover, the effect of using different irrigation solutions for wound lavage has also been investigated (19). To date, however, there have been relatively few studies that focused on assessing the clinical efficacy of PPL in human lower extremity wounds. Nourse and Myers (20), in 1978, showed the clinical efficacy of PPL on contaminated wounds in an area other than in the mouth, namely the sacrum. Since the initial studies in the 1970s, the use of PPL has gained acceptance as a useful method for irrigation of contaminated wounds at a number of different anatomical sites. In 1984, Diekmann (21) evaluated the healing rates of pressure ulcers that were either irrigated with a dental device or treated with "routine care," namely standard wound lavage using a bulb syringe. In that study, each group contained 4 matched groups based on wound size, and at the end of the 2-week experimental period, the PPL group showed a greater decrease in average wound size in comparison with the standard therapy group, although this difference was not statistically significant. In 1992, Chisolm (22) compared wound lavage techniques using a canister that delivered a lavage pressure of 8 pounds per square inch (psi) versus manual syringe irrigation for the management of acute lacerations treated at 2 Level I trauma center emergency departments. Chisolm (22) concluded that irrigation times were decreased when the pressurized canister was used, although there was no statistically significant difference between the infection rates in the 2 groups. Similarly, Morse (23) observed no statistically significant difference in infection rates for wounds lavaged with 1 of 4 different pressurized irrigation systems, ranging in pressure from 1.5 to 8.2 psi, used for the treatment of wounds managed in a Level II emergency department. Still further, Cervantes-Sanchez (24) undertook a randomized controlled trial (RCT) that compared systemic antibiotic therapy to the same antibiotic therapy plus wound lavage using a 20-mL syringe with a 19-gauge needle, and observed no statistically significant difference between the treatment groups in uncomplicated appendectomy wounds; however, a statistically significant decrease in postoperative infection was observed in the syringe and needle lavage group for complicated wounds that involved intraoperative findings indicative of gangrene, perforation, localized abscess, or diffuse peritonitis.

Recent studies have also evaluated the use of tangential hydrodissection for wound management. Granick et al (25) randomized 21 patients to either tangential hydrodissection or PPL for the treatment of a variety of wounds, although specific wound locations were not specified and diabetic and venous leg ulcers were excluded, and found that tangential hydrodissection and pulsed lavage reduced postdebridement bacterial counts by 90.8% and 86.9%, respectively. Mosti (26), moreover, compared tangential hydrodissection to local wound care with moist wound dressings for the management of chronic lower extremity ulcers, and found that tangential hydrodissection effectively decreased bacterial bioburden and the time required to achieve a "clean wound bed," although the definition of a clean wound bed was not clearly defined. Caputo (27) randomized 22 patients to tangential hydrodissection and 19 patients to wound debridement with PPL, for the management of lower extremity wounds, and showed statistically significant decreases in surgical time and the volume of saline used with the hydrodissection method; however, no statistically significant difference was observed in regard to wound healing.

To date there have been no published studies that we could find that evaluated the influence of PPL on the microbiology of infected lower extremity wounds. We hypothesized that PPL would alter the quantity of bacteria in lower extremity wounds and, in an effort to test this hypothesis, we undertook a prospective cohort study involving patients with lower extremity wounds that underwent operative debridement.

Patients and Methods

Patients were selected from the clinical practices of the Ankle and Foot Medical Centers of the Delaware Valley and the Emergency Department of Penn Presbyterian Medical Center, Philadelphia, Pennsylvania. Patients were admitted to the Penn Presbyterian. Medical Center for surgical management of their lower extremity wounds. To be included in the cohort, consecutive patients had to have a diagnosis of a lower extremity wound that was clinically considered infected or, in the case of an intact cutaneous barrier, suspected of underlying abscess, necrotizing fasciitis, myonecrosis, or osteomyelitis requiring surgical debridement. A successful outcome was defined as the absence of any microbiological organisms identified on the immediate postlavage wound culture. The following risk factors (independent variables) were selected prospectively and considered in the analyses: patient age and age category (< 40, $\geq 40 < 55$, $\geq 55 < 70$, $\geq 70 < 85$, and ≥ 85) in years; sex; body mass index (BMI; underweight, < 18.5; normal weight, 18.5 to 24.9; overweight, 25.0 to 29.9; obesity, ≥ 30.0); type of infection (none, cellulitis or erysipelas, abscess, necrotizing fasciitis or myonecrosis, osteomyelitis); ischemia, defined as the absence of at least one ipsilateral pedal pulse, either the posterior tibial or dorsalis pedis arterial pulse, on both manual and ultrasonic examination (yes or no); comorbidity (none, diabetes mellitus, peripheral arterial disease, chronic renal insufficiency or failure, diabetes mellitus plus any other disease, or any other disease); wound class, as described by the Centers for Disease Control and Prevention (28, 29) and depicted in Table 1; American Society of Anesthesiologists (ASA) physical status classification (30) as determined by the attending anesthesiologist and depicted in Table 2; University of Texas (UT) wound grade (31) (1, pre-ulcerative; 2, superficial wound; 3, tendon or joint capsule exposed; 4, bone or cartilage exposed); University of Texas wound stage (31) (A, clean; B, nonischemic but infected; C, ischemic; D, ischemic and infected); polymicrobial infection (yes or no); number of organisms seen on the prelavage and postlavage Gram stains (none, rare, few, moderate, many) (Table 3); morphology of organisms seen on the prelavage and postlavage Gram stains (gram-positive cocci, gram-negative rods, gram-positive cocci and negative rods, other, other plus gram-positive cocci and negative rods); number of organisms seen on the prelavage and postlavage cultures (none, few, moderate, many) (Table 3); morphology of organisms seen on the prelavage and postlavage cultures (methacillin-sensitive *Staphylococcus aureus*, methacillin-resistant *S aureus*, group B *Streptococcus*, *Pseudomonas*, *Bacteroides*, other flora); and whether or not the patient was already on a specific antibiotic based on culture and sensitivity results (yes or no). Specimens procured for microbiological assessments were maintained in standard transport tubes, and prepared and interpreted by certified laboratory technicians. Moreover, every specimen underwent microbiological assessments that included Gram stain analysis, as well as aerobic and anaerobic bacterial culture and sensitivity analyses. At the discretion of the operating surgeon, some specimens also underwent special staining and culture procedures, including periodic acid-Schiff and acid-fast stains, and inoculation on mycobacterial, chocolate, and fungal culture media.

The intervention involved surgical debridement of all grossly infected and necrotic soft tissue and bone. After gross debridement, the wound was vigorously lavaged using a commercially available PPL system (Pulsavac Plus System, Zimmer, Inc, Warsaw, IN) (Figure 1). Every time that the PPL was used, 3 liters of normal, sterile saline was flushed through the wound. Immediately before pulsed lavage, specimens were obtained from the deepest exposed surface of the wound for microbiological assessment using Gram stain and aerobic and anaerobic culture and sensitivity analyses. Immediately following pulsed lavage of the wound, additional specimens were obtained from the deepest exposed surface of the wound for Gram stain and aerobic and anaerobic culture and sensitivity analyses. As previously mentioned, a successful outcome was defined as the absence of any organisms identified on the immediate postlavage wound culture. As previously noted, all of the microbiological laboratory work was performed using standard transport tubes and carried out in the microbiology section of the clinical laboratory at the Penn Presbyterian Medical Center, Philadelphia, Pennsylvania.

Table 1
Centers for Disease Control and Prevention wound classification[28,29]

Classification (Risk of Infection)	Description of the Wound	Examples of the Type of Operation
Clean (low, 3%–5%)	Uninfected surgical wounds in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tracts are not entered. In addition, clean wounds are closed primarily and, if necessary, drained with closed drainage. Surgical incisional wounds that occur with nonpenetrating (eg, blunt) trauma should be included in this category if they meet the criteria.	Exploratory laparotomy, mastectomy, neck dissection, nonpenetrating blunt trauma, thyroidectomy, total hip replacement, vascular surgeries
Clean-contaminated (intermediate, 10%–80%)	A surgical wound in which the respiratory alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination. Specifically, procedures involving the biliary tract, appendix, vagina, and oropharynx are included in this category, provided no evidence of infection or major breaks in technique are encountered.	Bronchoscopy, cholecystectomy (any approach), laryngectomy, routine appendectomy, small bowel resection, transurethral resection of prostate, Whipple pancreaticoduodenectomy
Contaminated (high, > 80%)	Open fresh, accidental wounds. In addition, procedures that have major breaks in sterile technique (eg, open cardiac massage) or gross spillage from the gastrointestinal tract and incisions in which acute nonpurulent inflammation is encountered are included in this category.	Appendectomy for inflamed appendicitis, bile spillage during cholecystectomy, diverticulitis
Dirty-infected (already infected)	Old traumatic wounds that have 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 surgical field before the procedure.	Excision and drainage of abscess, myringotomy for otitis media, perforated bowel, peritonitis

The statistical plan entailed calculation of the incidence of a successful outcome (the absence of any organisms identified on the immediate postlavage wound culture) based on the number of cases included in the cohort. The data were collected by a single investigator (G.A.M.), and stored in a personal computer using Microsoft Excel 2004 for Mac, Version 11.3.7 (Microsoft Corporation, Redmond, WA). The data were analyzed by another investigator (D.S.M.) who did not participate in collection of the data, however served as one of the surgeons who performed some of the wound debridements. The analyses were performed using Stata 9.2/SE for Macintosh (Stata Corporation, College Station, TX). Attention was paid to the type and distribution of the data, and nonparametric tests of the null hypothesis were undertaken to identify differences between the number of bacteria present in the wound immediately before and after PPL, and to compare patient characteristics between wounds that displayed a successful outcome and those that did not; generalized estimation equations were used to explain the associations between independent variables and a successful outcome (32). A Greenland sensitivity analysis (33) was also undertaken to examine the resistance of the results to the influence of a hypothetical unmeasured variable. Statistical significance was defined at the 5% ($P \leq .05$) level for the analyses, except for those used to select independent variables for inclusion in the multiple variable regression equations, where statistical significance was defined at the 10% ($P \leq .1$) level to minimize the risk of excluding potentially important variables from the fully adjusted multiple variable regression models, which also included any other variables that the investigators considered clinically important regardless of the particular variable's univariate level of significance.

Results

Over the approximately 11-month period extending from October 11, 2006, to August 31, 2007, 73 cases in 55 patients met the criteria for inclusion in the investigation. Of these patients, 40 (72.73%) underwent a single wound debridement, 13 (23.64%) underwent 2 debridements, 1 (1.82%) underwent 3 debridements, and 1 (1.82%) underwent 4 debridements. The incidence of a successful outcome, namely the absence of any organisms identified on the immediate postlavage wound culture, was 69.86% (51/73 cases in 55 patients). A comparison of the number of bacteria on the immediate prelavage and immediate postlavage Gram stain and culture specimens was also undertaken to determine whether or not PPL decreased the quantity of bacteria in the wound, as determined by microscopic and microbiological analysis of the swab specimens, which showed that PPL resulted in a statistically significant decrease in the amount of bacteria identified by means of Gram stain ($P = .0004$) and bacterial culture ($P = .005$) (Table 4). In an effort to explain the observed results, we calculated the probability of the null hypothesis based on the prevalence of a number of demographic variables associated with the outcome (Table 5). With the exception of the morphology of organisms observed on the prelavage Gram stain, the quantity and morphology of the organisms observed on the postlavage Gram stain, and the organisms identified on the postlavage culture, none of the independent variables statistically significantly differed between those cases that achieved a successful outcome and those that failed to do so. That is to say, with the exception of the aforementioned independent variables (risk factors), the prevalences of all of the other risk factors that we took into consideration were not statistically significantly different between the group of cases that achieved a successful outcome (no organisms on the immediate postlavage culture) and those that did not.

In an effort to further evaluate the association of different risk factors with the outcome, and to make inferences related to the outcome based on the prevalences of the demographic variables, we used univariate and multiple variable generalized estimation equations (GEE) clustered on the patient, surgeon, and wound, to calculate the association (odds ratio) between the different independent variables and the outcome. We clustered the regression analyses because our data were not truly independent (35), in that some of the patients had more than one wound, the same surgeons treated some of the same patients, and some of the different bacteria came from the same wounds. The results of the univariate regression analyses (Table 6) showed that the presence of rare, few, moderate, or many organisms (as compared with no organisms) or gram-negative rods on the prelavage Gram stain specimen, as well as the growth of Group B *Streptococcus* on the prelavage culture, statistically significantly decreased the

Table 2
American Society of Anesthesiologists (ASA) physical status classification[30]

Class	Description of the Patient
1	Normal, healthy
2	Mild systemic disease, under control
3	Severe systemic disease
4	Severe systemic disease that is a constant threat to life
5	Moribund, not expected to survive without the operation
6	Declared brain-dead and organs harvested for donor purposes

None of the patients in the investigation described in this report were categorized as ASA class 5 or 6.

Table 3
Microbiological outcomes

Test	Description of Quantity	Number of Organisms
Gram stain	None	No organisms observed at any magnification
	Rare	< 1 organism per 1000x field, or < 10 organisms per entire smear
	Few	At least 1 organism per average 1000x field
	Moderate	2 to 10 organisms per average 1000x field
	Many	> 10 organism per average 1000x field
Culture growth on agar plate	None	No organisms observed on the agar plate
	Few	> 10 colonies in the first quadrant
	Moderate	< 5 colonies in the second quadrant of the agar plate
	Many	> 10 colonies in the first quadrant, > 5 in the second quadrant, and < 5 in the third quadrant of the agar plate

likelihood of achieving the outcome; whereas being of normal body weight (BMI 18.5–24.9) or obese (BMI > 30), as compared with being underweight; and being ischemic (University of Texas stage C), as compared to being neither infected nor ischemic; and showing gram-variable (neither gram-positive cocci nor gram-negative rods, or both), were statistically significantly associated with achieving the outcome. When the clinically and statistically important independent variables were loaded into a fully adjusted (multiple variable) equation, the results of the regression analyses (Table 7) showed that age 85 years or older and the presence of rare or many organisms (as compared with no organisms) and gram-negative rods on the prelavage stain statistically significantly decreased the likelihood of achieving the outcome; whereas, having a BMI indicative of normal weight and growth of few bacteria on the immediate prelavage culture were statistically

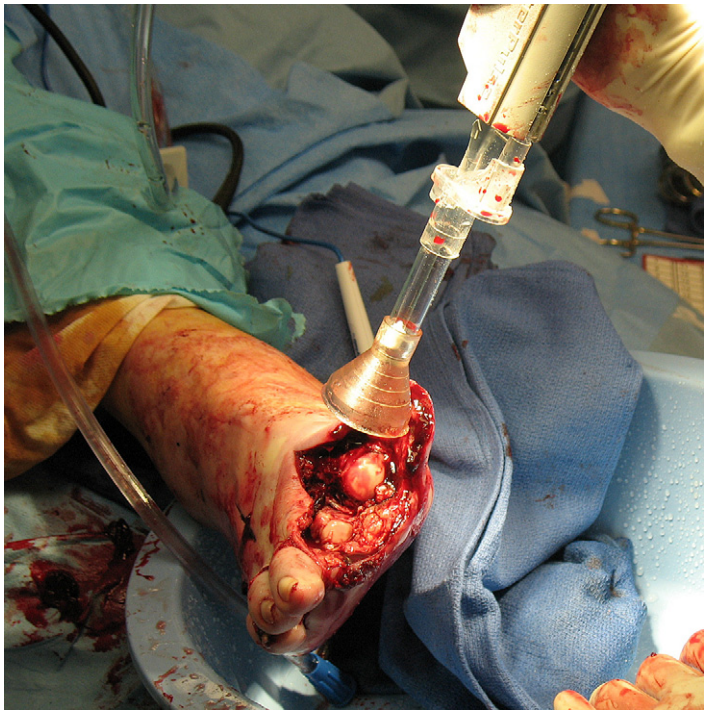

Fig. 1. Intraoperative view of power-pulsed lavage in forefoot debridement.

Table 4
Comparison of prelavage to postlavage bacterial counts on Gram stain and culture (N = 73 debridements in 55 patients)

Test		Prelavage, n (%)	Postlavage, n (%)	*P* Value*
Gram stain	None	43 (58.90)	56 (76.71)	.0004
	Rare	11 (15.07)	11 (15.07)	
	Few	12 (16.44)	4 (5.48)	
	Moderate	5 (6.85)	1 (1.37)	
	Many	2 (2.74)	1 (1.37)	
Culture growth on agar plate	None	17 (23.29)	22 (30.14)	.0050
	Few	9 (12.33)	19 (26.03)	
	Moderate	34 (46.58)	27 (36.99)	
	Many	13 (17.81)	5 (6.85)	

* Wilcoxon signed ranks test.

significantly associated with achieving the outcome. For most of the independent variables, the point estimates for the unadjusted (univariate) regression coefficients versus the adjusted (multiple variable) coefficients differed by more than 10% (Tables 6 and 7), suggesting that the effects of these variables were confounded (the independent variable had an influential association on another independent variable, both of which had influential associations with a successful outcome) by the other risk factors (32).

The following 2-way interactions (clinically reasonable combinations of independent variables) were also evaluated: age category and BMI category, wound category and prelavage Gram stain number and morphology, age and prelavage Gram stain number and morphology, and prelavage culture number and morphology, as well as BMI category and Gram stain number and morphology and prelavage culture number and morphology. Of these interaction terms, only the interaction of age category and prelavage Gram stain morphology and age category and prelavage culture morphology were statistically significant ($P \leq .05$). Although the precise clinical significance of these interactions is not fully clear, the effect estimates for the presence of gram-negative rods and *Bacteroides* on culture changed considerably as age category increased, and the CIs widened considerably, when the interaction terms were compared with the fully adjusted point estimates. Specifically, the interaction of age 70 years or older and gram-negative rods seen on the stain resulted in an odds ratio of 0.0336 (95% CI 0.0079, 0.7691), whereas the interaction of age 70 years or older and *Bacteroides* on the culture resulted in an odds ratio of 0.0656 (95% CI 0.00391, 0.7415). Using logistic regression and the sandwich variance estimator (a nonparametric estimator of variance), while clustering on patients (36–38), the likelihood ratio test showed the interaction of age 70 years or older and gram-negative rods seen on the stain, as well as the interaction of age 70 years or older and *Bacteroides* on the culture, to be statistically significant at $P = .0379$ and $P = .0084$, respectively. Effect estimates were also computed for linear combinations of coefficients, including the aforementioned interaction terms. These findings indicated effect modification (change in the measure of an association between an independent variable and the outcome variable, based on the presence of a third variable) between age category and BMI category, as well as between age category and the morphology identified using Gram stain, with both of these interactions decreasing the likelihood of achieving a result of no organisms seen on the immediate postlavage Gram stain. Clinically speaking, we feel that the interaction of age category and Gram stain morphology, as well as that of age category and the result of bacterial culture, are important in that they seem to suggest that the older the patient is with a lower extremity wound requiring surgical debridement, the more likely it is that gram-negative rods will be seen on the Gram stain, and the more likely it is that *Bacteroides* will be identified on culture, and these findings are associated with

Table 5
Prevalence of risk factors by outcome (N = 73 debridements in 55 patients)

Variable	Success* (n = 56 Cases)	Failure (n = 17 Cases)	*P* value†
Age, y (median, interquartile range)	52.5 (45, 64)	57 (49, 71)	.2346
Age < 40 y	10 (17.86)	3 (17.65)	.316
Age ≥40 < 55 y	20 (35.71)	5 (29.41)	
Age ≥55 < 70 y	17 (30.36)	4 (23.53)	
Age ≥70 < 85 y	8 (14.29)	3 (17.65)	
Age ≥85 y	1 (1.79)	2 (11.76)	
Male gender	38 (67.86)	9 (52.94)	.2639
Female gender	18 (32.14)	8 (47.06)	
BMI (median, interquartile range)	27.34 (22.11, 39.08)	26.09 (24.51, 27.12)	.2644
BMI < 18.5 (underweight)	1 (1.79)	2 (11.76)	.224
BMI 18.5–24.9 (normal weight)	20 (35.71)	4 (23.53)	
BMI 25.0–29.9 (overweight)	12 (21.43)	8 (47.06)	
BMI > 30 (obese)	23 (41.07)	3 (17.65)	
Diabetes mellitus	16 (28.57)	5 (29.41)	.281
Peripheral vascular disease	1 (1.79)	2 (11.76)	
Renal disease‡	4 (7.14)	4 (23.53)	
Diabetes mellitus + another	25 (44.64)	4 (23.53)	
Other systemic disease	10 (17.86)	2 (11.76)	
ASA 1 (normal, healthy patient)	0	1 (5.88)	.913
ASA 2 (mild systemic disease, controlled)	8 (14.29)	1 (5.88)	
ASA 3 (severe systemic disease)	39 (69.64)	12 (70.59)	
ASA 4 (severe systemic disease, life threatening)	9 (16.07)	3 (17.65)	
ASA 1 or 2 (normal, healthy or mild systemic disease)	8 (14.29)	2 (11.76)	.7926
ASA 3 or 4 (severe or uncontrolled systemic disease)	48 (85.71)	15 (88.24)	
Clean wound	17 (30.36)	6 (35.29)	.868
Clean-contaminated wound	16 (28.57)	4 (23.53)	
Contaminated wound	20 (35.71)	6 (35.29)	
Dirty wound	3 (5.36)	1 (5.88)	
Wound not clinically infected	7 (12.50)	1 (5.88)	.236
Cellulitis or erysipelas	7 (12.50)	1 (5.88)	
Abscess	13 (23.21)	3 (17.65)	
Necrotizing infection (fasciitis, myonecrosis)	4 (7.14)	3 (17.65)	
Osteomyelitis	25 (44.64)	9 (52.94)	
UT grade 1 (pre-ulcerative)	7 (12.50)	1 (5.88)	.236
UT grade 2 (superficial)	10 (17.86)	4 (23.53)	
UT grade 3 (tendon, joint capsule exposed)	11 (19.64)	3 (17.65)	
UT grade 4 (bone, cartilage exposed)	28 (50.00)	9 (52.94)	
UT stage A (clean)	8 (14.29)	1 (6.25)	.388
UT stage B (infected)	34 (60.71)	10 (62.50)	
UT stage C (ischemic)	2 (3.57)	0	
UT stage D (infected and ischemic)	12 (21.43)	5 (31.25)	
No organisms seen on Gram stain§	15 (26.79)	3 (17.65)	.759
Rare organisms seen on Gram stain§	8 (14.29)	1 (5.88)	
Few organisms seen on Gram stain§	26 (46.43)	10 (58.82)	
Moderate organisms seen on Gram stain§	5 (8.93)	2 (11.76)	
Many organisms seen on Gram stain§	2 (3.57)	1 (5.88)	
GPC seen on Gram stain§	15 (26.79)	7 (41.18)	.047
GNR seen on Gram stain§	0	1 (5.88)	
GPC and GNR seen on Gram stain§	2 (3.57)	4 (23.53)	
Other bacterial morphology seen on Gram stain§	39 (69.64)	5 (29.41)	
No growth on bacterial culture§	15 (26.79)	2 (11.76)	.110
Few growth on bacterial culture§	8 (14.29)	1 (5.88)	
Moderate organisms on bacterial culture§	24 (42.86)	10 (58.82)	
Many organisms on bacterial culture§	9 (16.07)	4 (23.53)	
MSSA on culture§	5 (8.93)	1 (5.88)	.522
MRSA on culture§	5 (8.93)	1 (5.88)	
Group B *Streptococcus* on culture§	0	1 (5.88)	
Pseudomonas on culture§	14 (25.00)	2 (11.76)	
Bacteroides on culture§	0	0	
Other single bacterial organism on culture§	6 (10.71)	4 (23.53)	
Polymicrobial growth on culture§	26 (46.43)	8 (47.06)	
No organisms seen on Gram stain‖	20 (35.71)	2 (11.76)	.011
Rare organisms seen on Gram stain‖	16 (28.57)	3 (17.65)	
Few organisms seen on Gram stain‖	19 (33.93)	8 (47.06)	
Moderate organisms seen on Gram stain‖	1 (1.79)	3 (17.65)	
Many organisms seen on Gram stain‖	0	1 (5.88)	
GPC seen on Gram stain‖	0	11 (64.71)	<.0001
GNR seen on Gram stain‖	0	2 (11.76)	
GPC and GNR seen on Gram stain‖	0	3 (17.65)	
Other bacterial morphology seen on Gram stain‖	56 (100)	1 (5.88)	
No growth on bacterial culture‖	20 (35.71)	2 (11.76)	.002
Few growth on bacterial culture‖	16 (28.57)	3 (17.65)	
Moderate organisms on bacterial culture‖	19 (33.93)	8 (47.06)	
Many organisms on bacterial culture‖	1 (1.79)	4 (23.53)	
MSSA on culture‖	3 (5.36)	1 (5.88)	.254
MRSA on culture‖	7 (12.50)	2 (11.76)	
Group B *Streptococcus* on culture‖	1 (1.79)	1 (5.88)	
Pseudomonas on culture‖	20 (35.71)	1 (5.88)	
Bacteroides on culture‖	0	1 (5.88)	
Other single bacterial organism on culture‖	10 (17.86)	3 (17.65)	
Polymicrobial growth on culture‖	15 (26.79)	8 (47.06)	
Culture-specific antibiotic therapy in effect	38 (67.86)	11 (64.71)	.8099

Values are n (%) unless otherwise indicated.
Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; GNR, gram-negative rods; GPC, gram-positive cocci; MRSA, methacillin-resistant *Staphylococcus aureus;* MSSA, methacillin-sensitive *Staphylococcus aureus*; UT, University of Texas.

* A successful outcome was defined as the absence of any organisms identified on the immediate postlavage culture.

† The Wilcoxon rank-sum test (Mann-Whitney 2-sample statistic) was used for comparing actual age, gender, body mass index, and whether or not culture-specific antibiotic therapy was in effect; otherwise, Cuzick's nonparametric test for trend (34) was used to test the null hypothesis across 3 or more ordered groups.

‡ Chronic renal insufficiency or failure.

§ Immediately before pulsed lavage.

‖ Immediately following pulsed lavage.

a greater likelihood of failure to achieve a finding of no organisms seen on the immediate postlavage wound culture.

Lastly, in an effort to take into consideration the possible influence of an unmeasured variable that could have potentially altered our results, we undertook a Greenland sensitivity analysis (33). To evaluate the resistance of our results to a theoretical unmeasured variable, we hypothesized the presence of an unmeasured confounding variable ranging in prevalence, in both the exposed and unexposed (relative to measured independent variables) groups, from 20% to 60%. The results of the sensitivity analysis (not shown) revealed that

Table 6
Univariate regression* results (N = 73 debridements in 55 patients)

Variable	Odds Ratio	95% Confidence Interval
Age ≥40 < 55 y	1.2	0.2431, 5.9245
Age ≥55 < 70 y	1.275	0.2444, 6.6515
Age ≥70 < 85 y	0.8	0.1244, 5.1432
Age ≥85 y	0.15	0.0096, 2.3361
Male gender	1.8765	0.6223, 5.6587
BMI 18.5–24.9 (normal weight)	10	1.7333, 57.6923†
BMI 25.0–29.9 (overweight)	3	0.6120, 14.7056
BMI > 30 (obese)	15.3333	2.3307, 100.8763†
Peripheral vascular disease	0.1563	0.0115, 2.1316
Renal disease§	0.3125	0.061, 1.6021
Diabetes mellitus + another	1.9531	0.4552, 8.3803
Other systemic disease	1.5625	0.2495, 9.7862
Diabetes mellitus	2.43	0.7953, 7.4228
ASA class 3 or 4	0.8	0.1641, 3.9001
Clean-contaminated wound	1.4118	0.3537, 5.6347
Contaminated wound	1.1765	0.3164, 4.3751
Dirty wound	1.0588	0.1679, 6.6774
Cellulitis or erysipelas	1	0.0628, 15.9372
Abscess	0.6191	0.0731, 5.2426
Necrotizing infection (fasciitis, myonecrosis)	0.1905	0.0204, 1.7758
Osteomyelitis	0.3968	0.0519, 3.0316
UT grade 2 (superficial)	0.3571	0.0323, 3.9528
UT grade 3 (tendon, joint capsule exposed)	0.5238	0.0462, 5.9369
UT grade 4 (bone, cartilage exposed)	0.4444	0.0471, 4.1982
UT stage B (infected)	0.425	0.0558, 3.2388
UT stage C (ischemic)	178.9342	16.6842, 1919.028†
UT stage D (infected and ischemic)	0.3	0.0300, 2.9989
Rare organisms seen on Gram stain‡	0.1231	0.0256, 0.5927†
Few organisms seen on Gram stain‡	0.1795	0.0375, 0.8592†
Moderate organisms seen on Gram stain‡	0.1429	0.0294, 0.7738†
Many organisms seen on Gram stain‡	0.0126	0.0159, 0.6616†
GNR seen on Gram stain‡	0.0072	0.0008, 0.0604†
GPC and GNR seen on Gram stain‡	0.0233	0.0335, 1.6266
Other bacterial morphology seen on Gram stain‡	3.64	1.0728, 12.3509†
Few growth on bacterial culture‡	1.0667	0.0772, 14.7429
Moderate organisms on bacterial culture‡	0.32	0.0542, 1.8908
Many organisms on bacterial culture‡	0.3	0.0406, 2.2194
MRSA on culture‡	1	0.0546, 18.3036
Group B *Streptococcus* on culture‡	0.0068	0.0003, 0.0123†
Pseudomonas on culture‡	1.4	0.092, 21.304
Bacteroides on culture‡	0.0734	0.0028, 1.8601
Other single bacterial organism on culture‡	0.3	0.0228, 3.9453
Polymicrobial growth on culture‡	0.65	0.0604, 6.99
Culture-specific antibiotic therapy in effect	1.1515	0.3868, 3.4281

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; GNR, gram-negative rods; GPC, gram-positive cocci; MRSA, methacillin-resistant *Staphylococcus aureus;* UT, University of Texas.

* Results via generalized estimation equation clustered on patient, surgeon, and wound.

† Result is statistically significant at the 5% level.

‡ Immediately before pulsed lavage.

§ Creatinine clearance < 80 ml/min.

the associations observed between the risk factor variable and the outcome were robust, as they resisted greater than 10% change in the presence of a theoretical, unmeasured confounding variable. For instance, in regard to the number of organisms observed on the prelavage Gram stain, the estimated odds ratio did not change more than 10% up to an odds ratio of nearly 12 for the unmeasured confounder relative to the outcome of interest.

Discussion

Main Effects

In this investigation, we defined a successful outcome as the absence of any organisms observed on the immediate postlavage culture, and the incidence of this outcome was 69.86%. Moreover, PPL statistically significantly decreased the amount of bacteria identified on the immediate postlavage specimens procured for Gram stain and bacterial culture analyses (Table 4, $P = .0004$ and $P = .005$, respectively). Overall, we observed 5 main effects, 3 of which decreased the likelihood of a successful (no organisms observed on the immediate postlavage culture) outcome, and 2 of which increased the likelihood of a successful outcome. The likelihood of a successful outcome was decreased if (1) the patient's age was 85 years or older; (2) rare or many organisms, as compared with no organisms, were identified on the immediate prelavage Gram stain; and (3) gram-negative rods were identified on the immediate prelavage Gram stain. The likelihood of a successful outcome was increased if (1) the patient's BMI was indicative of normal weight, and (2) few bacteria were identified on the immediate prelavage bacterial culture. This last observation, while being counterintuitive, we feel, was probably because of a more aggressive debridement before PPL, perhaps because the wound displayed a worse appearance because of the presence of the bacteria, or to conditions that predisposed to more bacteria being present, which led the surgeon to perform a more extensive prelavage debridement. Interestingly, the older the patient, the more likely it was that gram-negative rods would be identified on the Gram stain specimen, and the more likely it was that *Bacteroides* would be identified on culture, and these findings were associated with a greater likelihood of failure to achieve a successful outcome.

Confounding and Effect Modification

With the exception of the number of organisms observed on the prelavage bacterial culture, the point estimates for the unadjusted (univariate) generalized estimation equations (GEE) for age category, ASA physical status, UT stage, and prelavage Gram stain morphology, versus the fully adjusted (multiple variable) GEE, differed by more than 10%, suggesting that the effects of these variables were confounded by the other risk factors (32). Furthermore, several interaction terms were considered, and only the interaction of UT stage and the number of organisms observed on the prelavage Gram stain was statistically significant ($P \leq .05$). Although we are not completely certain as to the clinical significance of this interaction, the effect estimates for UT stage of 3 changed considerably and the CI widened when the interaction term was compared with the fully adjusted (multiple variable) point estimates. Further analyses clustered on patients (taking into consideration that our data were not truly independent, as some of the patients underwent multiple debridements) (36–38) showed the interaction of UT stage and the organism count on the prelavage Gram stain to be statistically significant ($P = .0031$). Effect estimates were also computed for linear combinations of coefficients, including the interaction terms. These findings indicated effect modification between UT stage and the number of organisms observed on the prelavage Gram stain, with this interaction decreasing the likelihood of observing no growth on the postlavage bacterial culture. Clinically speaking, we feel that the interaction of UT stage 3 and the number of organisms observed on the prelavage Gram stain is important in that it seems to suggest that an ischemic wound conveys more bacteria, as observed with Gram stain, and these factors were associated with a greater likelihood of failure to achieve no growth on the postlavage bacterial culture.

Sensitivity Analysis

The results (not shown) of the Greenland sensitivity analysis (33) revealed our effect estimates to be resistant to the potential influence

Table 7
Multiple variable regression* results (N = 73 debridements in 55 patients)

Variable	Odds Ratio	95% Confidence Interval
Age ≥40 < 55 y	31.6053	0.2273, 4395.321
Age ≥55 < 70 y	18.2575	0.1602, 2081.253
Age ≥70 < 85 y	2.4549	0.0113, 534.9529
Age ≥85 y	0.0108	0.0028, 0.4137†
BMI 18.5–24.9 (normal weight)	417.197	2.3867, 72926.64†
BMI 25.0–29.9 (overweight)	66.0074	0.483, 9020.819
BMI > 30 (obese)	3566.448	0.5691, 2237.45
Clean-contaminated wound	4.8903	0.1636, 146.2143
Contaminated wound	0.5418	0.0413, 7.1148
Dirty wound	5.079	0.1726, 149.4304
UT stage B (infected)	0.2847	0.006, 13.5335
UT stage D (infected and ischemic)	0.2198	0.0059, 8.1485
Rare organisms seen on Gram stain‡	0.0023	0.0001, 0.4243†
Few organisms seen on Gram stain‡	0.0049	0.0069, 3.4937
Moderate organisms seen on Gram stain‡	0.0064	0.0027, 2.1030
Many organisms seen on Gram stain‡	0.005	0.0002, 0.6816†
GNR seen on Gram stain‡	0.0085	0.00007, 0.026†
GPC and GNR seen on Gram stain‡	0.006	0.00002,
Other bacterial morphology seen on Gram stain‡	0.3345	0.0002
Few growth on bacterial culture‡	977094	1277, 75412†
Moderate organisms on bacterial culture‡	0.0166	0.0001, 2.9326
Many organisms on bacterial culture‡	0.6679	0.0014, 312.4308
MRSA on culture‡	63.4079	0.0025, 1637131.04
Group B *Streptococcus* on culture‡	0.0086	0.00003, 172.935
Pseudomonas on culture‡	0.0180	0.0001, 4.5074
Bacteroides on culture‡	0.1926	0.0018, 49.0027
Other single bacterial organism on culture‡	10.0075	0.0434, 2308.301
Polymicrobial growth on culture‡	60.1084	0.0554, 65173.74

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; GNR, gram-negative rods; GPC, gram-positive cocci; MRSA, methacillin-resistant *Staphylococcus aureus;* MSSA, Methacillin-sensitive *Staphylococcus aureus*; UT, University of Texas.

* Results via generalized estimation equations clustered on patient, surgeon, and wound.

† Result is statistically significant at the 5% level.

‡ Immediately before pulsed lavage.

of hypothetical independent variables. For instance, in regard to UT grade 3, the estimated odds ratio did not change greater than 10% up to an odds ratio of nearly 9 for the unmeasured confounder by the outcome. Similarly, in regard to identification of organisms on the prelavage Gram stain specimen, the effect estimate resisted significant change up to an odds ratio of greater than 9 for the unmeasured variable by the outcome. Therefore, the results or our investigation are robust and not likely to be changed by any reasonable unmeasured variables.

Limitations

Like most observational investigations, a number of methodological shortcomings influenced our results. Because the reduction in the amount of bacteria was measured in specimens procured immediately following debridement with PPL, it is very likely that the reduction was caused by the intervention. However, because we did not compare PPL to any other form of treatment, we are not able to tell whether the observed decrease in the amount of bacteria immediately following debridement with PPL was any more or less than it would have been following any other form of wound lavage. Furthermore, because this was an observational study, it could have been influenced by selection and information biases that may have affected the results and limited our ability to make valid conclusions. Although it is possible that bias affected the way in which risk factors were reported for different patients, we think that this form of information bias was unlikely to have taken place. Our main reason for this thinking is that the risk factors that we considered are fundamental to the surgical management of patients with lower extremity wounds requiring debridement. However, there may have been some selection bias, in that only 55 patients who underwent 73 debridements were included in the cohort. On an institutional level, this implies considerable selection bias; however, understanding that only 1 investigator (G.A.M.) collected data on consecutive cases in which he was personally involved, the potential influence of selection bias is better understood. In essence, all of the wound debridement cases in which the investigator was involved were enrolled into the study consecutively. As such, any bias would have been related to the investigator's involvement in the case. Because we felt that it was important to debride and lavage, and procure specimens, in a uniform fashion to minimize unmeasured variables, we feel that the benefits of having a single investigator associated with all of the cases outweighed any potential selection bias. Another potential shortcoming had to do with the possibility that the bacterial counts associated with swab cultures could have differed from the actual number of bacteria in the wound tissue. This potential discrepancy could not be overcome without procuring biopsy specimens and quantifying the number of bacteria per unit of tissue, and we feel that having done that would have diminished the generalizability of our findings. For this reason we used standard methods, common to every surgeon, to identify the presence of bacteria in the wound. Understanding, too, that only some of the specimens, at the surgeon's discretion, underwent more than just Gram stain and aerobic and anaerobic cultures, it is possible that we may have missed some microorganisms that would have required special staining or culture media to be adequately identified. Furthermore, we did not report histopathological diagnoses, such as osteomyelitis and necrotizing fasciitis, and the surgeon of record designated the wound type, which could have imparted some classification. Because our outcome of interest was the absence of bacteria on the immediate postlavage bacterial culture, we did not assess outcomes in histopathological terms, or in regard to the ultimate degree of wound healing. As such, we were not able to make any claims related to the efficacy of debridement with PPL in terms of wound healing.

Lastly, in observational epidemiology, the evaluation of risks and confounders (variables that influence other risk factors as well as the outcome) is limited to variables that are recorded in the dataset, and controllable confounding and random error account for only a portion of the total error. For these reasons, potential prejudices owing to classification errors, selection biases, and unmeasured confounders need to be considered in the interpretation of the results. In other words, our results could have been affected by the influence of unmeasured variables that some surgeons may consider important in regard to wound debridement and microbiology, including such risk factors as wound location and wound size. Therefore, we hypothesized the presence of an unmeasured independent variable that ranged widely in regard to prevalence and its association with the measured risk factors and the outcome, and observed our effect estimates to be resistant to change even when the likelihood (odds ratio) of experiencing the outcome in the presence of the unmeasured confounder, as compared with the likelihood in the absence of the unmeasured confounder, was as great as an odds ratio of 12. For this reason, we feel that the results of this study, and the conclusions that we formed, are resistant to the potential influence that unmeasured variables may have had.

In conclusion, 73 cases in 55 consecutive patients were enrolled in an effort to determine the influence of PPL on lower extremity wound microbiology in association with surgical debridement. The main outcome was defined as "successful" if no organisms grew on culture agar from a swab culture performed immediately after PPL of a debrided lower extremity wound. A successful outcome was achieved in 51 (69.86%) of the 73 cases, and debridement plus PPL statistically significantly decreased the bacteria count between the

immediate prelavage and immediate postlavage specimens, as measured with Gram stain ($P = .0004$) and by counting colonies on bacterial growth agar ($P = .005$). After all of the analyses were performed, we noted that the following main effects were associated with a decreased likelihood of observing no organisms on the immediate postlavage culture: (1) patient's age 85 years or older, (2) rare or many organisms on the immediate prelavage Gram stain, and (3) gram-negative rods on the immediate prelavage Gram stain; whereas the following main effects were associated with an increased likelihood of observing no organisms on the immediate postlavage culture: (1) BMI indicative of normal weight, and (2) few bacteria on the immediate prelavage culture specimen. We feel that foot and ankle surgeons can use the results of this investigation in a number of ways. For instance, patients 85 years or older, and those who display rare or many organisms, or gram-negative rods, on the prelavage Gram stain, are likely to require multiple debridements or longer local care and systemic antibiotic therapy to achieve satisfactory clinical results, because it is likely that bacteria will persist in the wound following debridement with PPL. Moreover, we feel that the gross clinical appearance of a clean wound bed, as well as a Gram stain that shows rare organisms, can be misleading, because even the presence of rare organisms on the Gram stain was associated with a statistically significant decrease in the likelihood of achieving a successful outcome. Finally, because the absence of any microorganisms identified on the immediate postlavage culture specimen was observed 69.86% of the time, relying solely on postlavage swab cultures may lead to inadequate treatment of wounds that continue to be contaminated. For this reason, we recommend that surgeons treating such wounds maintain careful surveillance of the healing process, and adjust therapy based on periodic reassessment of the appearance and microbiology of the wound.

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