The Risk of Infection and Indication of Systemic Antibiotics in Chronic Wounds

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ABSTRACT

Background. No definitive guidelines exist to assist clinicians in determining when a chronic wound is infected or at risk for infection, nor do guidelines exist to aid in determining the indication or duration of systemic antibiotics. The lack of widely accepted guidelines can lead to excessive and improper use of systemic antibiotics, which can contribute to adverse drug events and the rise of multidrug-resistant organisms. Implementing a simple tool to measure the risk of infection in patients with chronic wounds could help clinicians determine the indication and appropriate use of systemic antibiotics as well as potentially reduce the use of systemic antibiotics. **Objective.** This evidence-based practice project aims to identify both chronic wounds at risk for infection and the risk factors associated with chronic wound infection, evaluate the use of systemic antibiotics in patients with chronic wounds, and reduce the use of systemic antibiotics in chronic wounds that are not infected or at risk for infection by implementing a Wounds at Risk (WAR) score for all patients admitted with chronic wounds. **Materials and Methods.** In this pre- and post-observational study, a convenience sample of all patients admitted with chronic wounds over a 6-week period were given a WAR score based on electronic medical record observations. Data were collected on the use and indication of systemic antibiotics and were compared with the same data of a control group of patients admitted with chronic wounds during a 6-week period before project implementation. Other clinical, microbiological, and demographic data also were collected and compared between the 2 groups. **Results.** Though not significant, the overall use of systemic antibiotics was decreased in the post-intervention group. A significant reduction was seen in wound-related indications for antibiotics, most notably in the "infected ulcer" category. Diabetic foot ulcers were at highest risk for infection, and pathogen or microbiological burden did not play a significant role in infection risk. **Conclusions.** The WAR score can help guide clinicians in determining the need for antibiotics, thus helping to reduce unnecessary antibiotic exposure, which can reduce the incidence of adverse drug events and multidrug-resistant organisms.

KEY WORDS

chronic wounds, wounds at risk for infection, systemic antibiotics, infection, antimicrobial stewardship

INDEX

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Up to 2% of the US population has a chronic wound, including diabetic foot ulcers (DFUs), venous leg ulcers (VLUs), arterial ulcers, nonhealing surgical wounds, and pressure ulcers/injuries (PU/Is).[1,2] Chronic wounds are associated with a significant increase in health care utilization and health care costs,[3] increased morbidity and mortality,[4] and decreased quality of life.[5] In addition, patients with chronic wounds have more exposure to systemic antibiotics compared with patients without chronic wounds, putting them at a higher risk for developing multidrug-resistant organisms (MDROs) and other adverse events.[6] Because of this, it is vital for health care providers to identify when a chronic wound is at risk for infection to avoid both the overuse and underuse of systemic antibiotics. Despite this, no widely accepted guidelines exist to assist clinicians in determining when a chronic wound is infected or at risk for infection, nor do definitive guidelines exist to aid the clinician in determining the indication or duration of systemic antibiotics.[7,8] This ambiguity can lead to excessive and improper use of systemic antibiotics, which then contributes to adverse drug events (ADEs) and the development of MDROs in not only the patient but also in the community.[8] The Wounds at Risk (WAR) score is a tool used to assess the risk of infection in patients by scoring a number of host factors that can contribute to an increased risk for infection in wounds. Implementing this simple tool could help clinicians determine the indication and appropriate use of systemic antibiotics and potentially reduce the use of systemic antibiotics in this patient population.

Economic, health, and social burden of multidrug resistant organisms

Each year, 23 000 deaths and more than 2 million illnesses are caused by MDROs.[9] The number one risk factor for developing an MDRO is previous exposure to antibiotics.[8] Up to 60% of patients with chronic wounds are treated with at least 1 systemic antibiotic within a 6-month period despite a lack of evidence to support the benefits or efficacy of systemic antibiotics for chronic wound healing rates.[10] A direct relationship exists between the overuse of antibiotics and the rise of MDROs, making routine and even "last resort" antibiotics ineffective.[8] Contamination of normal skin flora and colonization of bacteria, including MDROs, is a natural occurrence in wounds and especially in chronic wounds.[11-13]

Antibiotics can be harmful. Even when prescribed and taken properly, antibiotics can cause ADEs, including super infections like *Clostridioides difficile* colitis and severe—and sometimes fatal—reactions like Stevens-Johnson syndrome and anaphylaxis.[8,9] In the United States, antibiotics are responsible for nearly 1 out of every 5 ADEs seen in emergency departments and each year, the United States sees 250 000 cases of *C difficile*, resulting in 14 000 deaths annually.[9]

Varied risk factors for infection

The Infectious Diseases Society of America (IDSA), the British Society for Antimicrobial Chemotherapy, and the European Wound Management Association all concur that no universally accepted diagnosis criteria for an infected chronic wound exists.[7,8,14] They also agree that the traditional signs and symptoms of infection include redness (erythema/rubor), warmth (calor), purulence, swelling or induration (tumor), and tenderness and pain are not always present in infected chronic wounds.[8,14] In fact, in the IDSA's guidelines for the diagnosis and treatment of diabetic foot infections, the presence of at least 2 of these symptoms is enough to both diagnose a diabetic foot infection and treat with systemic antibiotics, but the authors of the guidelines warn that these diagnostic criteria are based solely on expert opinions and not evidence.[14]

MATERIALS AND METHODS

Project design

One avenue explored in adult patients with chronic wounds was asking how the implementation of a WAR score for all patients admitted with chronic wounds affects the use of systemic antibiotics compared with adult patients with chronic wounds receiving usual care in patients not at increased risk for infection. By implementing a WAR score for all patients admitted with chronic wounds over a 6-week period, this evidence-based practice project aimed to: (1) identify chronic wounds at risk for infection; (2) identify the risk factors associated with chronic wound infection; (3) evaluate the use of systemic antibiotics in patients with chronic wounds; and (4) reduce the use of systemic antibiotics in chronic wounds that are not infected or at risk for infection.

Data from a control group of all patients also admitted with chronic wounds during the 6-week period before project implementation were collected for the WAR score and other data comparison with the implementation group. Data were collected from a convenience sample of all adult patients over the age of 18 years admitted with a chronic wound(s) present on hospital admission in a 325-bed acute care hospital in Texas. *Chronic wounds* were defined as wounds present for at least 3 weeks and included DFUs, VLUs, arterial ulcers, nonhealing surgical wounds, and PU/Is. A total of 57 patients made up the pre-intervention/control group, and 78 patients were included in the intervention group (N = 135).

The WAR score

In 2010, an international group of wound experts created the WAR score to better assess the risk of infection in chronic wounds by evaluating both the actual wound and host factors that can contribute to an increased risk of infection.[12,15,16] The risk factors in the WAR score incorporate the patient's immune status, including acquired immunosuppressive diseases (eg, diabetes, HIV), immunosuppressive therapies (eg, glucocorticoids, other chemotherapies), systemic hematological diseases that can affect the inflammatory response, occupational and social conditions, wound location and likelihood of contamination, the patient's age, and the type and chronicity of the wound, among other factors.[12,15,16]

The tool uses a simple screening scale (**Table**) to score the risk of infection in wounds by scoring each risk factor. The listed risk factors for infection are represented by 1, 2, or 3 points; a score over 3 justifies the use of systemic antibiotics, as it indicates an increased risk for infection. Patients with a score at or below 3 are not at an overall increased risk for infection; therefore, the use of antibiotics is not clearly indicated. Though not used as an absolute indicator, the tool can guide decision-making for both novice and expert wound care clinicians.[15]

In their official guidelines for the management of chronic wounds, the Polish Wound Management Association recommends the WAR assessment tool when evaluating a patient with a chronic wound.[15] In 2018, the International Society of Antimicrobial Chemotherapy (formerly known as the International Society of Chemotherapy for Infection and Cancer), the Chronic Wound Initiative, Austrian Society for Infection Control, Organization of all German-speaking Societies and Groups in Wound Management, and the German Society for Hospital Hygiene published a consensus report for antiseptic and antimicrobial recommendations in wound care using the WAR score as the primary assessment tool to help clinicians in deciding the appropriateness and indications for topical antiseptic wound therapy or systemic antibiotics.[16]

Other risk factors for infection in chronic wounds

Risk factors for infection in chronic wounds also were measured before and after project implementation. The risk factors noted in the WAR score were used to collect retrospective data on the risk factors of those patients found to have high WAR scores (≥4), compared with other demographic and clinical information. Examples include the prevalence of diabetes, microbiological burden and pathogen, and wound measurements, if obtained.

The measured bacterial burden and potential pathogen(s) of chronic wounds play a significant role in determining bacterial colonization versus bacterial infection in wounds.[13,17] *Pseudomonas* and methicillin-resistant *Staphylococcus aureus* (MRSA) are common pathogens found in chronic wounds, but do not necessarily cause true

Table. WAR score

RISK CLASS	RISK CONDITION	YES	Per Risk: 1 Point
1	Acquired immunosuppressive disease (eg, diabetes mellitus)		
	Acquired immune defect due to medical therapy such as cyclosporine, methotrexate, glucocorticoids, or antibodies		
	Solid tumor disease		
	Systemic hematological disease		
	Postsurgical wound healing disorder, which results in (unplanned) secondary healing		
	Problematic hygienic conditions related to social or occupational environment		
	Patient age >80 years		
	Young patient age (premature infants and infants)		
	Wounds persisting >1 year		
	Wound dimensions >10cm²		
	Chronic wounds of any etiology having a depth of >1.5cm		
	Extended inpatient status >3 weeks		
			Per Risk: 2 Points
2	Severe acquired immune defects (eg, HIV infection)		
	Heavily contaminated acute wounds		
	Bite, stab, and gunshot wounds penetrating 1.5cm–3.0cm		
			Per Risk: 3 Points
3	Severe innate immunodeficiency (eg, Wiskott-Aldrich syndrome, DiGeorge syndrome, immunodeficiency after stem cell transplantation, AIDS, immunosuppressive therapy)		
	Traumatically contaminated wound after debridement		
	Wounds that have a direct connection to organs or functional structures (eg, joints) or which contain foreign material (eg, prothesis)		
		Total Score:	

WAR Score ≤3: Patient *not* at increased for wound infection; systemic antibiotics may NOT be indicated
WAR score ≥4: Patient is at increased risk for wound infection; systemic antibiotics may be indicated

WAR: Wounds at Risk for infection

infection.[12] Jockenhöfer et al[12] noted that most of the patients with chronic wounds had the presence of both *Pseudomonas* and MRSA, and especially in those patients with a WAR score of less than 3.

Procedure

Internal review board approval was obtained from the University of Texas at Arlington and from the project site hospital through the Medical Research and Medical Executive Committees. In addition, informational in-services were provided to nursing staff in the wound care department and medical-surgical floors.

All patients with wounds present for at least 3 weeks who were admitted to the hospital between November 5, 2018, and December 13, 2018, were given a WAR score based on data obtained from the electronic medical records (EMRs). A copy of the patient's specific WAR scoring tool was placed in the patient's physical chart, and a note was written in the patient's EMR as a progress note. Based on the patient's WAR score, the EMR note read:

- "WAR scale score ≤ 3: patient not at increased risk for infection; systemic antibiotics may not be indicated"; or
- "WAR scale score ≥ 4: patient at increased risk for infection; systemic antibiotics may be indicated."

Simultaneously, data were collected on the use and indication of systemic antibiotics and other clinical data, including wound measurements, type of wound, microbiological burden and pathogen (if culture was obtained), and demographic data. A retrospective chart review was completed of patients admitted with chronic wounds during the 6 weeks prior to project implementation. These patients were given a WAR score based on the information from the EMR, and the same clinical and demographic data also were collected. No patient identifying information was collected or stored. Patients in the intervention group were identified by the date of recruitment and the patient number. Patients in the control group were identified by the date of admission and the subsequent patient number.

RESULTS

WAR scores and antibiotic use

During their hospital stay, 85% of the total sample population (N = 135) received systemic antibiotics. The overall use of systemic antibiotics decreased by 7.7% in the post-intervention group (P = .163) (**Figure 1**), despite a similar mean WAR score in both the pre-intervention and post-intervention groups (2.77 and 2.79, respectively). The distribution of WAR scores among both groups varied from 0 to 7, with most (69.7%) being less than or equal to 3 or not at increased risk for infection (**Figure 2**). At least 51% of the patients in both groups had exposure to systemic antibiotics in the previous 6 months; 63% of these patients had received the antibiotics in the month prior to hospital admission. Of note, 8 of these patients were infected with, or had a recent history of, *C difficile* colitis.

The indications or diagnoses for antibiotic use were divided into 9 categories: 3 represented "wound-related" indications (infected ulcer, cellulitis, and osteomyelitis) and the other 6 represented "non-wound-related" indications (urinary tract infection [UTI], pneumonia, bacteremia, sepsis, other, and no indication given) (**Figure 3**). Overall, wound-related indications for systemic antibiotics decreased by 23.8% (from 59.6% to 35.8%) in the post-intervention group, and the non-wound-related indications for antibiotics increased by 23.7% (from 40.4% to 64.1%) in the post-intervention group (P < .01). Specifically, UTI indications for antibiotic treatment increased by 5.3%, pneumonia increased by 9.1%, bacteremia increased by 2%, and the "no indication given" category increased by more than 9%. A significant reduction (P = .049) in the indication "infected ulcer" was noted in the post-intervention group, but no other significant reductions were noted in individual wound-related indication groups. For example, in the post-intervention group, cellulitis decreased by 3.2% and osteomyelitis decreased by 6.5%.

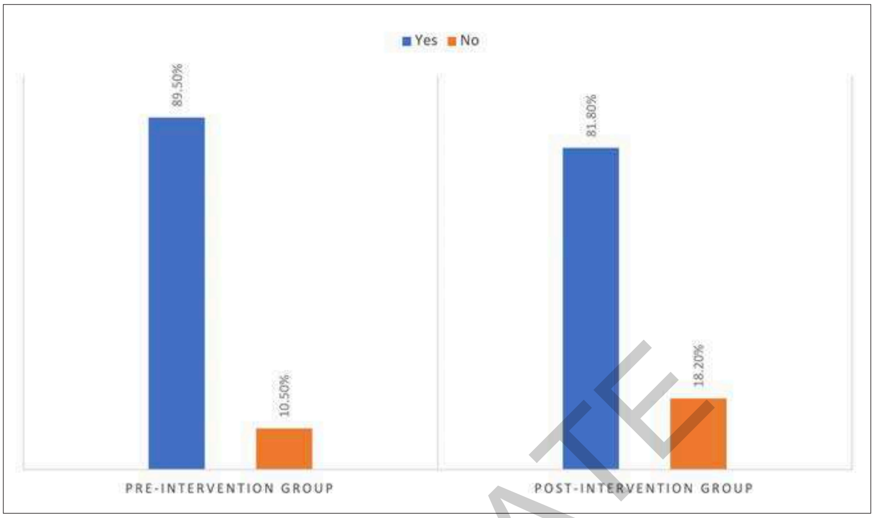

Figure 1. The overall use of systemic antibiotics.

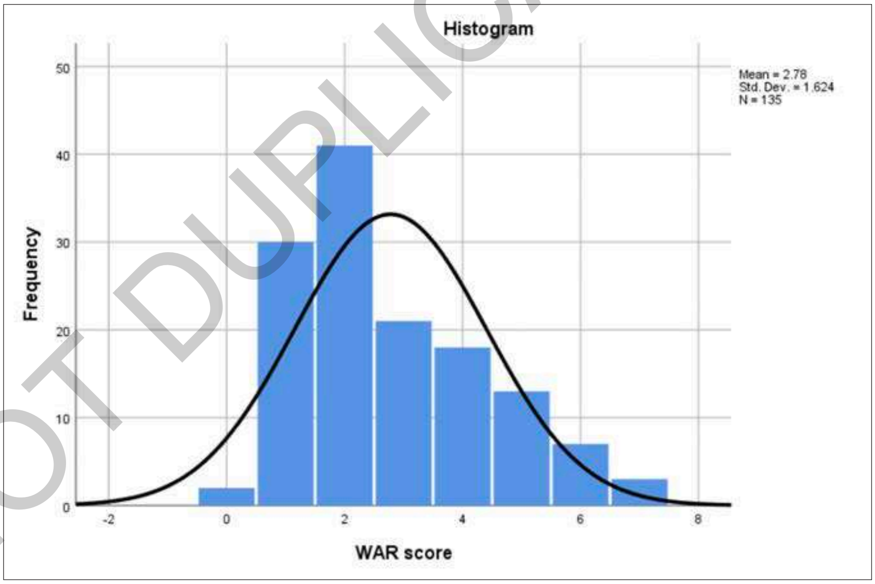

Figure 2. Distribution of WAR scores.
WAR: Wounds at Risk of infection; Std. Dev: standard deviation

The overall distribution of wound types varied; PU/Is made up the majority of chronic wounds (44.8%), DFUs were 30.6%, followed by VLUs, nonhealing surgical wounds, ischemic ulcers, and arterial ulcers (14.9%, 11.9%, 0.03%, and 0.01%, respectively) (**Figure 4**). Despite the overall higher prevalence of PU/Is, patients with DFUs comprised most of the patients with high WAR scores (18%), compared with 10% of PU/Is with a WAR score over 3 (P < .01). Nonhealing surgical wounds and venous and ischemic ulcers remained at a low prevalence in the high WAR-scoring group. Age distribution and wound type or etiology showed a distinction between patients aged 69 years and under and 70 years or older. Diabetic foot ulcers dominated the wound type in those under 70 years of age, and PU/Is were most prominent in patients 71 and older (**Figure 5**).

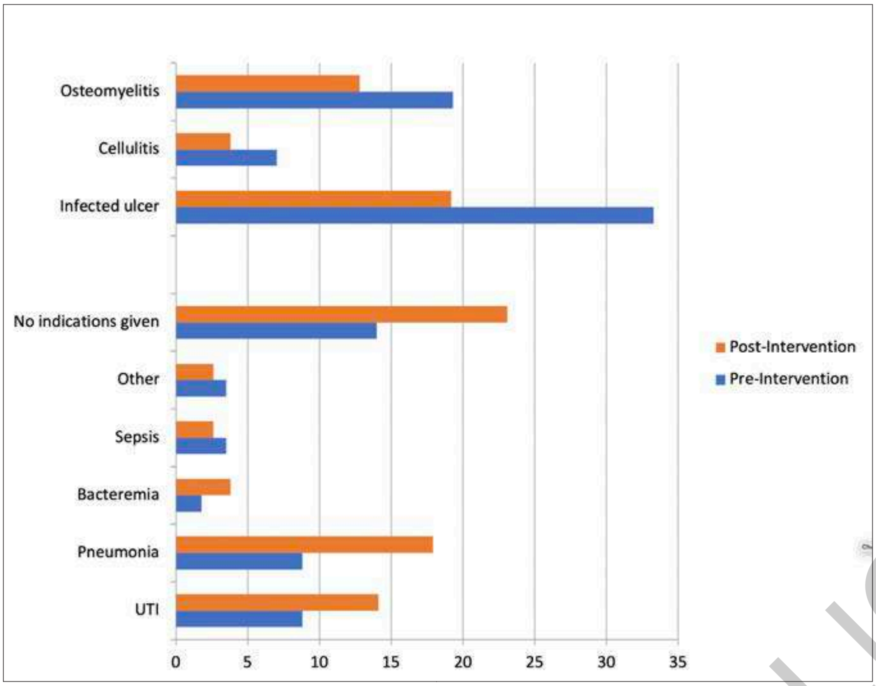

Figure 3. Indications for antibiotic use before and after WAR score implementation.
WAR: Wounds at Risk of infection; UTI: urinary tract infection

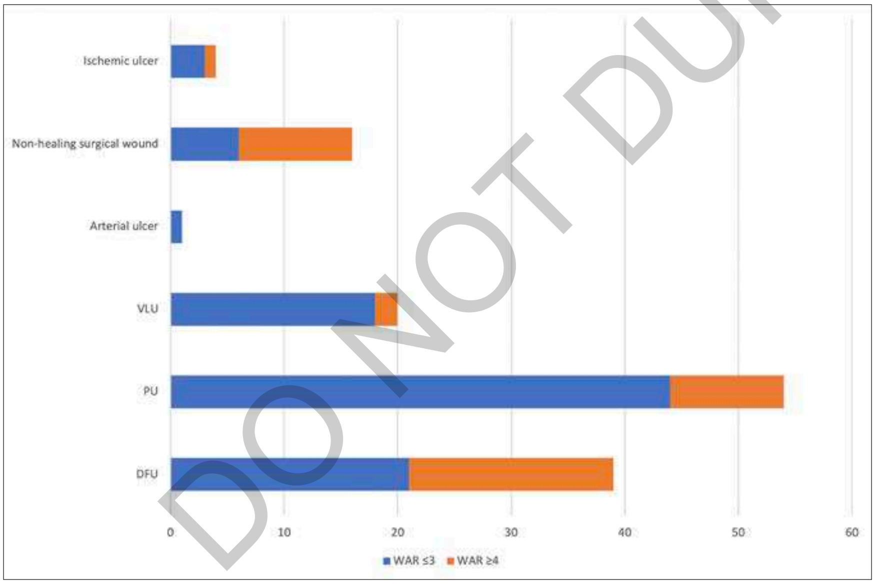

Figure 4. Types of wounds versus WAR scores.
WAR: Wounds at Risk of infection; VLU: venous leg ulcer; PU: pressure ulcer; DFU: diabetic foot ulcer

Microbiology

Wound cultures were obtained in about 25% of the patients admitted with an existing wound (22.2%) and, if positive, results were given by pathogen type and pathogen burden (low, moderate, or heavy). A total of 40% of wound cultures were of low microbiological burden, 30% moderate, and 16.7% heavy growth; in 13.3%, no pathogen was isolated. The mean WAR score stayed relatively the same across microbiological burden variables, with the exception of wounds without pathogen isolate (negative culture), which had a mean WAR score of 4.75, compared with 3.5, 3.8, and 3.4 for the low, moderate, and heavy microbiological growths, respectively.

Multidrug-resistant organisms made up 36.7% of all isolates (including extended spectrum beta-lactam [ESBL]-producing *Escherichia coli*, MRSA, and *Acinetobacter*). Further differentiation of the total isolates showed 26.7% with MRSA, 20% with *P aeruginosa*, 16.7% with methicillin-sensitive *S aureus* (MSSA), and 33.3% with polymicrobial species, including normal skin flora. The isolated pathogens had no significance on bacterial load or burden; MRSA and MSSA were found in all burden groups, and *P aeruginosa* was not found in the heavily burdened wounds (**Figure 6**).

Demographics

Demographic variables with a direct positive correlation to a high WAR score (≥4) included males (70% vs. 30%), patients with diabetes ($P < .001$), and an age range of 56 to 70 years (**Figures 7–9**).

DISCUSSION

WAR scores and antibiotic use

Although no statistical significance was noted in the total use of systemic antibiotics in the pre-intervention and post-intervention groups ($P = .163$), it is clinically significant considering the sample size and the timeframe of the implementation. If the project had continued over a year, for example, with the same trend, it would likely lead to a significant decrease in the use of antibiotics. This does seem to help answer the question of whether the WAR score can help reduce the use of inappropriate or unnecessary antibiotics for non-infected wounds or wounds that are not at risk for infection, even though no statistical significance was noted in the implementation period, given the small sample size and time limitations.

In both groups, most patients (69.7%) had a WAR score equal to or less than 3, meaning the majority of these chronic wounds were not at an increased risk for infection. Despite this, almost 60% of the pre-intervention group had a wound-related indication for antibiotic therapy, but this number significantly dropped to 35.8% after the implementation of the

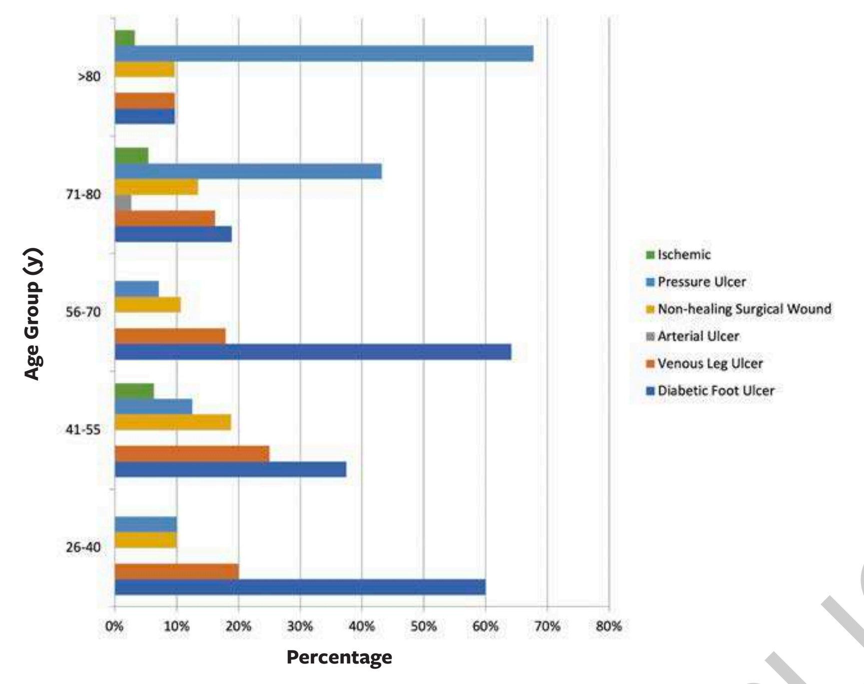

Figure 5. Age groups versus wound types/etiology.

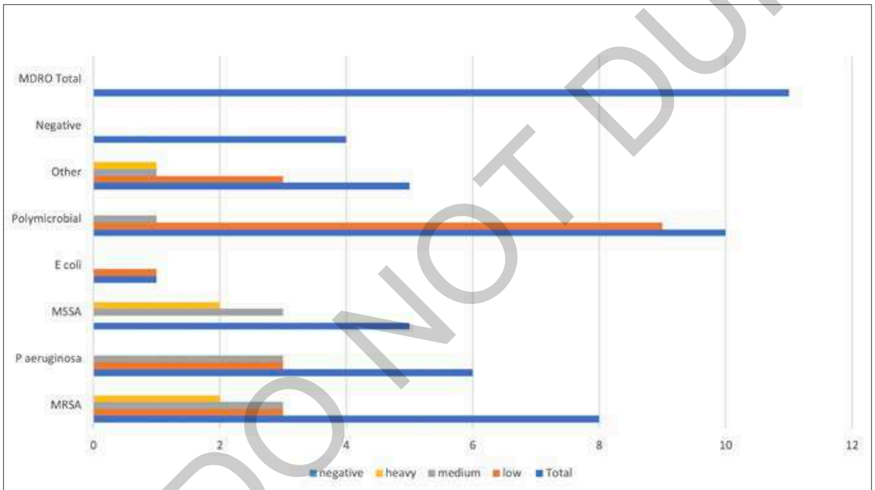

Figure 6. Microbiological data.
MDRO: multidrug-resistant organisms; *E coli: Escherichia coli*; MSSA: methicillin-sensitive *Staphylococcus aureus*; *P aeruginosa: Pseudomonas aeruginosa*; MRSA: methicillin-resistant *Staphylococcus aureus*

WAR score ($P < .01$), and conversely, the non-wound-related indications increased by 23.7% after WAR score implementation ($P < .01$). This could be explained by an increased awareness, by providers, of risk factors associated with the likelihood of chronic wound infection or the unwillingness to have a competing diagnosis with a low WAR score, which is emphasized by the significant reduction in the antibiotic use indication of "infected ulcer" in the post-intervention group ($P = .049$).

Another explanation for the significant increase in non-wound-related indications for antibiotics in the implementation group could be the time of year. During the winter months, an increase in patients admitted for the diagnosis of pneumonia can often be observed in acute care hospitals.[18] In the post-intervention group, the diagnosis of pneumonia (both community-acquired and hospital-acquired) was 28.6%, compared with only 17.6% in the pre-intervention group (an 11% increase in the post-intervention group). This argument, however, does not account for the simultaneous decrease in wound-related indications, as no previous studies have suggested that a certain season or time of year typically affects wound infection rates.

Diabetic foot ulcers and PU/Is are known to increase both morbidity and mortality,[2] and both also are associated with multiple and prolonged courses of antibiotics,[4] whether indicated or not. Data from this project suggest chronic DFUs are more prone to infection than chronic PU/Is. Almost half of the chronic wounds of the sample patients were PU/Is (44.8%) compared with 30.6% of chronic wounds attributed to DFUs. Despite the overall higher prevalence of PU/Is in the sample group, DFUs were more likely to be at risk for infection. A total of 18% of the patients noted to have high WAR scores (≥ 4)—thus at an increased risk for infection—had DFUs compared with only 10% of patients with high WAR scores with PU/Is. This should be considered with the probability that many chronic PU/Is are also at high risk for wound contamination due to the typical localization of PU/Is in the sacral and/or ischial regions, oftentimes in patients who are immobile and incontinent.[19] This higher risk for infection in DFUs could be contributed to the relative decreased circulation to the lower extremities compared with the thoracic or sacral areas and to the immunosuppressive factors attributable to diabetes.[20,21]

Similar to previous studies[6,8,12] on the use of antibiotics in chronic wounds, most (at least 51%) of the patients in the total sample population had been exposed to antibiotics in the previous 6 months, many of whom had received multiple parenteral courses before admission.

Microbiology

Although wound cultures were only obtained in a small percentage of patients in the sample group, it is noted that neither the microbiological burden nor the isolated pathogen had a significant correlation with infection risk. Surprisingly, the highest WAR mean values in both groups were without an identified isolate from the culture. Most of these did, however, have a positive Gram stain, which underscores the fact that no wound is sterile, and all wounds fall under the categories of contaminated, colonized, critically colonized, or locally infected. Cultures should not necessarily be used to screen for infection but rather to guide antimicrobial decision-making in infected wounds.

As the data from the present study and previous studies[12,13] show, obtaining sensitive cultures from chronic wounds can be problematic. Due to most of the sample patients in this study having received antibiotics in the weeks or months prior to hospital admission, many of whom had received multiple courses of antibiotics in the previous months, the microbiome of the wound would change and not be completely trustworthy. Like previous studies,[12,13,17] MDROs comprised the majority of the isolated pathogens from these chronic wounds (36.7%), including ESBL-producing pathogens and MRSA. Furthermore, of the isolated pathogens from the cultured wounds, 33% were polymicrobial, 26.7% were MRSA, 16.7% were MSSA, and 20% were *P aeruginosa*.

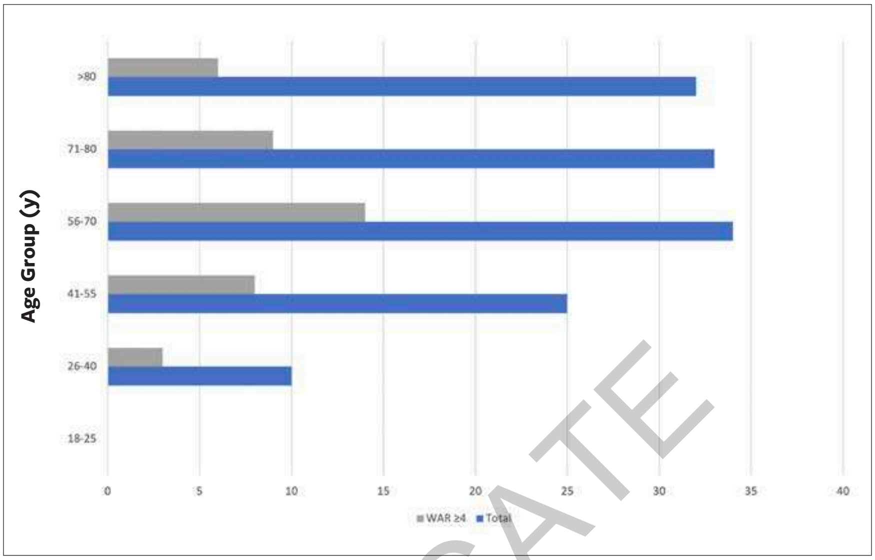

Figure 7. Age and WAR score.

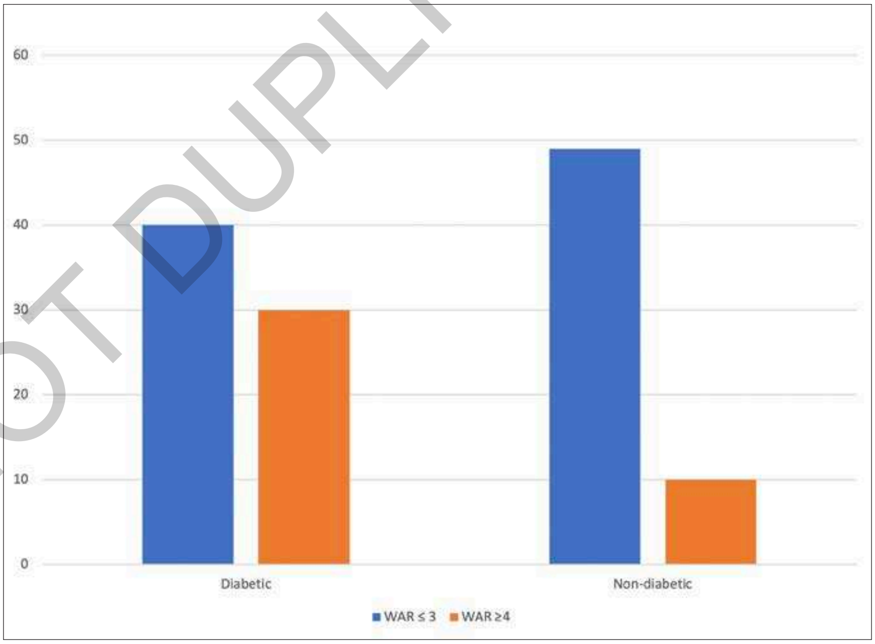

Figure 8. Diabetes and WAR score.

Demographics

A somewhat surprising finding was the age that correlated most to a high WAR score. Despite that a risk point was added for patients over the age of 80 years, the age group of 56 to 70 years old had a slightly higher risk for infection than any other age group. Males were more likely to have a higher WAR score (70% vs. 30%), and patients with diabetes had a significantly higher risk for infection ($P < .001$). No other significant findings were noted in the WAR score risk factors.

LIMITATIONS

Several limitations were noted throughout this project. The use of a convenience sample and the sample size itself (N = 135) limited the validity of the studied variables, as did the short 6-week intervention period. As noted, the statistical significance of decreasing the overall use of systemic antibiotics may well have been observed in a sample size of at least 500, but with only 135 patients over a 6-week period, only a clinical significance was noted. Time constraints also limited the data collection on wound closure and wound healing rates in each of the groups.

Using EMRs as the only observable mechanism to fill out the WAR score severely limited the researchers' data and quite possibly may have affected the potential WAR scores. For example, the researcher had to depend on the reliability of the wound measurements given in the EMR, and only 53% of the wounds had measurements available in the EMR, which may have affected WAR scores if they were available.

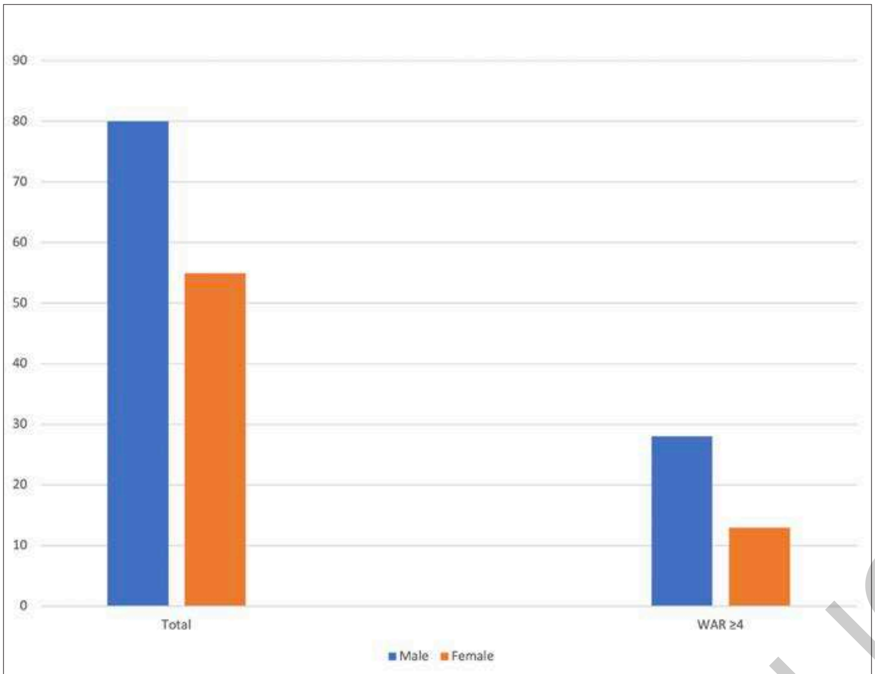

Figure 9. Sex and WAR score.

Last, the project site was also a limitation due to the acuity of many of the patients, which affected the overall indications for systemic antibiotics, like acute pneumonia, UTI, bacteremia, and other acute illnesses that require systemic antibiotics. A skilled nursing facility, nursing home, or even an outpatient primary care office or home health service would have been the most appropriate project site for using the WAR score to help determine the need for systemic antibiotics in patients who are not acutely ill.

Implications

The WAR score emphasizes the need to consider not only the wound appearance and presentation, but the entire patient, including immune status, age, social factors, wound chronicity, and other holistic factors. Without sufficient guidelines to assist clinicians in deciding whether to start or continue antibiotics for a chronic wound, a score to help guide these decisions can help reduce both the underuse and overuse of antibiotics and potentially reduce the incidence of ADEs related to antibiotic use, including the development of MDROs at a local level. The WAR score also can help to raise awareness to the fact that all wounds are contaminated, and the use of systemic antibiotics in even critically colonized wounds is not indicated in most chronic wounds. Most chronic wounds benefit from local antiseptics and aggressive wound care management.[8,22,23]

This project implies, that at the very least, providers and other medical staff would benefit from education on the current treatment recommendations for chronic wounds without signs or symptoms of systemic infection and without increased risk for infection. A facility-based guideline for patients admitted with chronic wounds, with the implementation of the WAR score, could help decrease the overall use of systemic antibiotics. In addition, this project helped support other research and raise awareness on the importance of obtaining previous antibiotic history when considering to repeat the same antibiotic treatment without clear evidence suggesting previous attempts had helped to close a chronic wound. The watch-and-wait approach in wounds that are not at increased risk for infection, together with aggressive wound care management, should be the standard approach to the care of chronic wounds.

CONCLUSIONS

The social, health, and economic burdens of chronic wounds are an astounding and growing problem in the United States as well as a major threat to the public health of Americans. Patients with chronic wounds are at an increased risk for morbidity and mortality, and they also are more likely to be exposed to unnecessary antibiotics, which is the leading cause of acquiring of MDROs. Using the Model for Evidence-Based Practice Change, this DNP project implementation of a WAR score for patients admitted with a chronic wound aimed to determine if the WAR score helped to decrease the overall use of systemic antibiotics in chronic wounds not at risk for infection, identify risk factors for infection in chronic wounds, and evaluate the use of systemic antibiotics in chronic wounds. The data analysis did show that awareness was raised and a decrease in the overall use of antibiotics was noted in the intervention group, though not significant over the limited timespan of the project. Despite this, the analysis does support the use of a WAR score to help clinicians determine the risk for infection and deciding on the appropriateness of systemic antibiotics and the importance of raising awareness of this issue.

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