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Single-Dose First-Generation Cephalosporin for Extremity Gunshot Wounds Offers Sufficient Infection Prophylaxis

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Abstract: Antibiotic prophylaxis for extremity gunshot wounds (GSWs) is highly variable. The objective of the present study is to quantify the adherence rate to a protocol for single-dose cephalosporin prophylaxis for extremity GSWs and the impacts on post-injury infection rates. We reviewed patients presenting to a level 1 trauma center with an extremity gunshot wound between 2019 and 2021. Infection rates were compared for patients following the protocol or not, and for patients presenting before or after the protocol's implementation. Overall, 94% of patients received antibiotic treatment at presentation, but only 34% followed the single-dose antibiotic protocol. The rate of protocol adherence increased from 15% to 39% after the protocol was implemented in the hospital in January 2020 (p = 0.081). Infection rates were not different before and after the protocol implementation (25% vs. 18%, p = 0.45). Infection rates were also not different between patients who did and did not follow the protocol (15% vs. 20%, p = 0.52). The implementation of a single-dose cephalosporin protocol increased adherence to the protocol in a level 1 trauma center without increasing infection rates. These findings support conservative treatment along with a single dose of first-generation cephalosporin antibiotic for uncomplicated extremity GSWs in order to decrease healthcare costs without compromising infection risk.

Keywords: extremity gunshot wound; cefazolin; prophylaxis

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1. Introduction

Firearm fatality rates in the United States (U.S.) reached a 28-year high in 2021, representing a 45.5% increase since 2004 [1]. There were over forty-five thousand firearm-related deaths in the U.S. in 2020 alone. Nonfatal gunshot wound (GSW) injuries have seen a similar rise of 41% from 2014 to 2018 [2]. Accordingly, civilian GSW injuries are increasingly common reasons for presentation to emergency rooms across the country. Nearly half of GSWs involve the extremities, with mortality and post-injury complications, including infections, representing a significant burden of injury [3–5]. Additionally, every emergency room visit, procedure, and admission for extremity GSWs incurs a cost for both patients and hospital systems. GSWs can create a wide range of injuries, from superficial wounds to complex soft tissue, bone, and neurovascular injuries. These skin-penetrating injuries create a risk of infection, and prophylaxis against infection should accordingly be considered. In order to minimize infection and healthcare costs and to optimize outcomes, orthopedic surgeons should standardize antibiotic prophylaxis protocols for extremity GSW patients. In particular, in level 1 trauma centers serving populations with high rates of firearm violence, guidelines for antibiotic therapy would streamline emergency department courses for patients and standardize decision making for providers.

There is no current standard of care regarding antibiotic use for extremity GSWs, both for GSWs treated operatively and for those treated nonoperatively [6–9]. To address the risk of infection after GSW injury, most studies recommend that such injuries be treated with some form of antibiotics; this is reflected in the high rates of antibiotic use after extremity GSWs, which range from 88% to 91% [10,11]. However, there remain large variations in the type and number of antibiotics selected, as well as in dosing and duration. Frequently recommended antibiotics include first- and third-generation cephalosporins, gentamycin, amoxicillin/clavulanic acid, and other penicillin types [10,12–14]. There is limited literature available to help guide antibiotic choices for extremity GSWs. In the absence of recent data to guide antibiotic selection, the variability in prophylactic management will continue to persist.

In addition to variability in antibiotic prophylaxis, extremity GSW patients undergo a wide range of treatments, from simple to invasive. Naturally, the different injury patterns seen with GSW injuries necessitate different treatment strategies. As is particularly seen with open or complex fractures, many GSW injuries require operative intervention for orthopedic fixation. Operatively treated GSW fractures also typically receive perioperative antibiotics, adding an additional layer of complexity to how GSW injuries are treated prophylactically to prevent infections [15]. Traditionally, orthopedic surgeons have opted to manage GSW injuries as akin to open fractures, with antibiotics on presentation and incision and drainage surgery within 24 h. This means that several extremity GSW patients end up in an operating room for, at minimum, a washout debridement surgery in attempts to minimize infection risk [10,13,16–20]. Naturally, since extremity GSWs often come from the trauma mechanisms of injury, expediting the time from presentation to intervention is indeed warranted for some patients. There is also some thought that high-velocity GSWs require immediate extensive debridement; however, low-velocity GSWs may be managed with superficial debridement only, with or without antibiotic prophylaxis [10,13]. Furthermore, previous studies have demonstrated that some fractures secondary to low-velocity GSWs may be treated nonoperatively [9]. Using open-fracture management guidelines, there may thus be a subset of extremity GSW patients who undergo operations that are not necessary for either injury treatment or infection prevention. Additionally, some of these operations are unnecessarily expedited in order to fall within the 24 h from the presentation window.

Recent studies have evaluated the outcomes of implementing a standardized single-dose protocol for antibiotic use after extremity GSWs in a level 1 trauma center. A 2017, a retrospective review found that patients receiving a single dose of intravenous (IV) antibiotics for GSW injury without fracture showed a 20% absolute-risk reduction of infection compared to those who did not receive antibiotics [8]. This research was followed by a prospective study which implemented the protocol for single-dose IV first-generation cephalosporin within one hour of presentation to a level 1 trauma center emergency room for extremity GSWs. That study found a protocol adherence rate of 67%, with a 14% lower infection rate in patients who followed the protocol compared to a control group who received no antibiotic prophylaxis [15]. Another prospective study reported a 62% adherence rate to a protocol for single-dose cefazolin or amoxicillin/clavulanic acid prophylaxis following GSWs. The researchers found that their protocol decreased infection risk by 14% [14]. In addition to reducing infection risk after extremity GSW, such a protocol can prevent unnecessary hospitalizations and use of resources, saving on healthcare costs. One study found that a single-dose antibiotic protocol saved an average of USD 1436 per patient [21]. Another potential harm of overusing antibiotics for the treatment of GSWs includes building antibiotic-resistant microbial strains. Thus, antibiotic use for GSW patients should ideally reflect the minimum dose and duration required to sufficiently protect against infection.

The present research was conducted to assess the generalizability of a successful single-dose IV first-generation cephalosporin protocol for extremity GSWs to other level 1 trauma centers. Accordingly, the antibiotic protocol evaluated herein was modeled

after the protocol in the aforementioned articles [8,15]. Where oral antibiotics rely on patients' treatment adherence and filling the prescription after discharge, IV antibiotics ensure compliance, especially among the trauma patient population where follow-up can be unreliable. The present study aims to include the defining injury characteristics of extremity GSW patients, and to report treatment courses including operative management, adherence to the single-dose antibiotic protocol, and rates of infection or other complications. The hypothesis was that after the protocol implementation, adherence rates to the protocol would increase and be associated with lower rates of infection.

2. Materials and Methods

With Institution Review Board approval, a retrospective review was conducted on patients who presented to a level 1 trauma center between January 2019 and October 2021. The dataset included skeletally mature patients with one or multiple GSWs to an extremity, including the pelvis, with a follow-up of at least two weeks. Charts were selected from the electronic medical record by filtering for date range, mention of extremity GSW, and involvement of orthopedic or plastic surgery departments. Notably, this research included extremity GSWs from a variety of injury mechanisms, ranging from accidental self-inflicted injuries to gun violence. All GSWs were classified as low-velocity or low-energy civilian GSWs. All the filtered charts were manually reviewed to create the final dataset according to predetermined inclusion and exclusion criteria. Specifically, emergency department documentation including consultation notes and operative reports, as well as clinical follow-up notes, were reviewed. Exclusion criteria included involvement of the head, neck, thoracic or abdominal cavity, a high-energy or high-velocity mechanism of injury, initial presentation and workup in an outside emergency department, lack of involvement of orthopedic surgery or plastic surgery departments, and presentation for complications of old, non-acute GSWs.

The single-dose first-generation cephalosporin protocol was initiated by the orthopedic surgery department at our trauma center in January 2020. The protocol was introduced to representatives from the emergency department and the trauma acute care team. After agreement with these teams on the protocol's implementation, provider education was performed. Evidence supporting the protocol was disseminated in multidisciplinary team meetings.

Patient demographics, injury characteristics, information on the antibiotics administered, and outcome data were collected via retrospective chart review using the electronic medical records. Demographics included age, sex, Body Mass Index (BMI), diabetes diagnosis, alcohol and illicit drug use, smoking status, and homelessness. Injury characteristics included the anatomic location of the GSW(s), the number of GSWs, details about the mechanism of injury, and the time of injury and presentation to the emergency room. Additionally, any concomitant fractures and nerve or vascular injuries were noted.

To understand antibiotic use among the GSW patients and calculate compliance rates with the protocol implemented in January 2020, the timing of antibiotic administration, number of antibiotics given, type of antibiotic(s), and dosing information were recorded. The management of the GSWs was noted, and any surgeries performed to address bony or soft tissue injuries were recorded. Finally, the date of the last follow-up with our hospital system was recorded. The reported outcomes included any bony or infectious complications noted during clinical follow-ups related to the GSW injury throughout March 2022. Post-injury infections were defined as erythema, purulent drainage, abscess, osteomyelitis, or a need for additional antibiotic administration. This encompassed both superficial and deep infections.

Descriptive data analyses were conducted to quantify demographic trends, injury patterns, antibiotic usage, and post-injury infection rates in the entire dataset. The data were then separated into two separate cohorts to divide the patients presenting prior to or after January of 2020, which was the date of protocol initiation in our trauma center. Demographics and injury patterns were then analyzed in each group and compared in

order to ensure that both groups were comparable and reduce suspicion of confounding variables driving results.

Post-injury infection rates and bony complications were compared across the pre-protocol and post-protocol groups with relative risk calculations. Additionally, the dataset was split according to patients who did and did not follow the protocol, and comparative analyses were performed to interpret the effect of protocol adherence on infection rates. Data were evaluated with 2-tailed Student's t-tests, chi-square tests with or without Yates correction, and Fisher's exact test where appropriate using Microsoft Excel (Microsoft 365, Redmond, WA, USA) and GraphPad (Graphpad Software 9, La Jolla, CA, USA). Statistical significance was defined as $\alpha < 0.05$.

3. Results

A total of 185 patients with extremity GSWs who presented to our emergency department between January 2019 and October 2021 were identified in the electronic medical record, and their charts were carefully reviewed. Of these, 99 met the inclusion criteria and were considered in the final analyses. Ninety-three percent of patients were male, the average age was 31 $\pm$ 13 years, and the average BMI was 27 $\pm$ 6 kg/m^2. There were 42 patients who reported current tobacco use, 49 patients who did not use tobacco, and 8 with unknown tobacco-use status. Furthermore, 51 patients reported current alcohol use, 38 patients reported no alcohol use, and 10 had unknown alcohol use. Twenty-two patients reported substance use including cannabis, heroin, amphetamines including methamphetamine, and cocaine use. Seventy-six patients did not report drug use, and one patient's drug-use status was unknown. Only two patients in the dataset had diabetes; both had type II diabetes. There was also one patient with recorded prediabetes. There were four patients who were experiencing homelessness at the time of their presentation to our emergency department.

Twenty-two patients presented with multiple GSWs, with an average of 1.3 GSWs per patient. Fifty-seven (58%) GSWs were to the lower extremities, and forty-five (45%) were to the upper extremities. There were forty-eight (48%) left-sided injuries, forty-four (44%) right-sided injuries, and seven (7%) bilateral GSWs. Seventy-nine patients with fractures were identified. Of those seventy-nine, fifty-seven required fixations for an overall fracture rate of 80% and a fixation rate of 72%. Concomitant vascular injuries were found in twenty-three (23%) patients, and nerve injuries were found in thirty-two (32%) patients. These demographic trends were similar in the subset of patients presenting before (pre-protocol) and those presenting after (post-protocol) the protocol was initiated in our level 1 trauma center (Table 1).

Overall, ninety-three (94%) patients received antibiotics upon presentation to the emergency department; however, only thirty-four (37%) of those patients followed the single-dose IV first-generation cephalosporin protocol. The average number of antibiotic doses given to patients who received antibiotics but did not adhere to the protocol was 7.6 doses, with a range of 2 to 40 doses. There was a total of seventeen infections detected, with an overall infection rate of 17%. Infection rates were not significantly different between patients who did and did not follow the protocol; patients who followed the antibiotic protocol had an infection rate of 15% compared to 20% among those who were noncompliant with the protocol (RR = 0.735, 95% CI [0.29, 1.89]). Bony complications were seen in eleven (11%) patients.

Twenty patients were treated prior to the protocol implementation in January 2020. Of this subset, nineteen (95%) received antibiotics, though only three received a single-dose of a first-generation cephalosporin. Of the remaining seventeen patients, one did not receive any antibiotics, one received vancomycin, three were discharged with a course of an oral first-generation cephalosporin, and the remaining twelve received multiple doses of a first-generation cephalosporin in the hospital (Table 2). In this pre-protocol group, five patients (25%) had an infection: three with cellulitis, two with osteomyelitis, and one with an abscess. One patient had a bony non-union.

Table 1. Patient demographics and characteristics.

	Pre-Protocol	Post-Protocol	*p*-Value	Total
Number of patients	20	79		99
Age	29.8	31.1		31
Gender (% Male)	19M; 1F (95%)	73M; 6F (92%)	0.65	92M; 7F (93%)
Injury location (UE = upper extremity, LE = lower extremity)	9 UE; 13 LE	36 UE; 44 LE		45 UE; 57 LE
Number GSWs	1.2	1.35		1.3
Concomitant fracture	16 (80%)	62 (78%)	0.88	78 (79%)
Fracture requiring fixation	12 (75%)	47 (76%)	0.95	59 (76%)
Antibiotics (any)	19 (95%)	74 (94%)	0.81	93 (94%)
Followed antibiotic protocol	3 (15%)	31 (39%)	0.081	34 (37%)
Infection	5 (25%)	14 (18%)	0.45	17 (17%)

Table 2. Antibiotics prescribed.

Pre-Protocol (*n*)	Post-Protocol (*n*)
cefazolin (18)	cefazolin (65)
vancomycin (1)	cephalexin (10)
cephalexin (1)	penicillin (7)
bacitracin (1)	sulfamethoxazole-trimethoprim (1)
	ertapenem (1)
	clindamycin (1)
	metronidazole (1)
	bacitracin (1)

Seventy-nine patients presented with an extremity GSW after the protocol was implemented. In this post-protocol group, seventy-four (94%) received antibiotics, of which thirty-one (42%) received the recommended single-dose first generation cephalosporin. Of the forty-eight patients who did not follow the protocol, five did not receive any antibiotics, seven received a penicillin, ten were discharged with a course of an oral first-generation cephalosporin, and sixteen received multiple doses of a first-generation cephalosporin in the hospital (Table 2). The post-protocol group had fourteen infections, with an infection rate of 18%. There were ten total bony complications in this group, including six non-unions, two of which required surgical repair, one hardware failure, one requiring hardware removal, and one with evidence of heterotopic ossification.

In comparing the pre-protocol and post-protocol cohorts, higher rates of adherence to the single-dose cephalosporin protocol were seen after the protocol was implemented in January 2020. However, this difference did not reach statistical significance under an alpha value of 0.05 (RR = 2.6, 95% CI [0.89, 7.69], $p = 0.081$). Similar rates of infection were seen in the pre-protocol and post-protocol cohorts (RR = 0.71, 95% CI [0.29, 1.74], $p = 0.45$).

4. Discussion

The purpose of this study was to evaluate the protocol of single-dose IV first-generation cephalosporin for extremity GSW injuries implemented in a level 1 trauma center. The primary aims were to quantify the adherence to the protocol and to quantify the rates of infection and bony complications for extremity GSW patients. The secondary aims

included detailing the patient and injury characteristics, such as concomitant bone and neurovascular injuries, as well as documenting surgical interventions. Our hypothesis was that adherence to the prophylactic antibiotic protocol would increase after the protocol was officially implemented in our trauma center, and that this would be associated with a decreased infection rate. A primary goal of this research was to provide data to help orthopedic surgeons to standardize their management of extremity GSWs in order to optimize recovery and minimize costs. This would help to reduce the currently quite high amount of variability in antibiotic strategies for GSW injuries and standardize this management across trauma centers in the U.S.

The single-dose antibiotic recommendation discussed herein was mirrored after similar guidelines on the treatment of extremity GSWs used in other level 1 trauma centers in the U.S. [8,21]. Studies on this protocol in those settings have shown promise both for reducing infection rates up to 14% and for minimizing healthcare costs with an average of USD 1436 savings demonstrated per patient [8,15,21]. The results of our retrospective research corroborate these previous findings and support a widespread adoption of a single dose antibiotic protocol for extremity GSW management guidelines. Initiation of the protocol in our trauma center was agreed upon by the emergency, trauma, and orthopedic departments. Provider education on the protocol was performed, and information on the literature supporting the protocol was shared in multidisciplinary team meetings.

In our ninety-nine patients, the overall adherence to the protocol was 34% and the overall infection rate was 17%. A comparison of the demographic data between the pre-protocol and post-protocol groups confirms that our study cohorts were comparable. This increases our confidence that the differences in protocol adherence and infection rates were the effects of the protocol initiation in our trauma center and lowers suspicion of confounding.

The protocol implementation in January 2020 led to a 2.6-fold increase in adherence to the recommended IV antibiotic prophylaxis regimen. There was also a 1.4-fold decrease in infection rate, from 25% before the protocol implementation to 18% post-implementation, though this was not a statistically significant difference. Thus, adherence to the protocol was not associated with an increased infection risk. This finding indicates that the recommended antibiotic and conservative care did not sacrifice the quality of infectious outcomes after extremity GSWs. Together with the current literature on this topic, the available data indicate that implementing and following a protocol for single-dose cephalosporin antibiotic prophylaxis for extremity GSWs sufficiently protects against or even reduces infection and can prevent unnecessary hospital stays and antibiotic orders to save an average of USD 1436 per patient [8,14,15,21].

Our data also reveal that fractures are often seen as secondary to low-velocity extremity GSWs. Furthermore, the majority of such fractures are treated with operative fixation. Therefore, a significant proportion of patients' hospital courses involve admission for surgery versus being taken directly to the operating room from the emergency department. These operative cases notably receive prophylactic perioperative antibiotics according to surgical protocols. The important distinction for these patients is that the additional antibiotics given perioperatively were indicated for their fracture and their operative fixation, rather than for the extremity GSWs as a pattern of injury itself.

Historically, providers have opted to treat GSW injuries according to the standard practice for open fractures: antibiotics within one hour of presentation and irrigation and debridement surgery within 24 h of presentation in order to decrease the risk of infection [10,13,16–20]. Typical antibiotics for an open fracture include a first-generation cephalosporin, with added gentamycin for grade 3 Gustilo–Anderson fractures. A penicillin is also indicated for injury mechanisms that raise suspicion of anaerobic infections, such as farm injuries [12]. Despite the widespread historical management of GSWs with operative debridement within 24 h, the recent literature suggests that this more aggressive strategy may not be indicated for low-velocity civilian extremity GSWs [10,13,22]. In the absence of a strong indication for extensive debridement, such as intra-articular fracture or pelvic

fracture with concomitant bowel injury [10], an operation may add unnecessary time, risks, and costs to patients' care without providing any substantial benefit. Accordingly, more recent orthopedic research, including the present study, supports a shift towards providing prophylactic antibiotics in the emergency department and clinical follow-up for patients presenting with uncomplicated extremity GSWs [8,10,15].

Beyond saving on money, time, and resources, preventing unnecessary antibiotic use has clear benefits given the known harms of over-prescribing antibiotics. First, even low-toxicity antibiotics like cephalosporins have known side effects including nausea, vomiting, diarrhea, and abdominal pain. Additionally, any antibiotic use presents an opportunity for building antibiotic resistance. Thus, from an antibiotic stewardship standpoint, minimizing antibiotic use to only what is needed for infection coverage or prevention is ideal.

Adopting this protocol also offers the chance to prevent operative management of less-complex GSW injuries. Under this protocol's guidelines, if a patient does not have another indication for surgery such as fractures requiring fixation or neurovascular injury requiring operative treatment, they do not need to be taken to the operating room for debridement. The protocol also eliminates the 24 h deadline for operative debridement, meaning that the urgency of surgeries can be determined on a case-by-case basis. This protocol can thus reduce patients' exposure to surgeries and prevent nonessential operations, thereby reducing hospital stays and avoiding the risks of anesthesia and surgery.

Our study is not without limitations. First, the research design was retrospective, meaning that the collectable data were limited by the information present in completed charts. Additionally, this research considered uncomplicated extremity GSWs only, without abdominal, chest, or head involvement, and only GSWs that were low-velocity mechanisms of injury. Our results also represent civilian GSW patients only. These limitations should be considered when evaluating the generalizability of the results. However, our findings do align with previously reported outcomes. This increases the confidence in our ability to support the efficacy of this antibiotic protocol in optimizing outcomes and minimizing costs for extremity GSW patients.

Our recommended antibiotic protocol features a simple design that would be reasonably cheap, quick, and easy to implement across different sites. For optimal protocol initiation, we would recommend communication between emergency departments and trauma care departments, as well as orthopedics teams and education providers. The present research offers additional data to support the protocol and should be shared with providers in order to encourage protocol adoption. These efforts should encourage prompt adherence to the protocol.

Following of this protocol has previously been associated with decreased infection rates. Additionally, this protocol is associated with significant resource savings, as patients have previously received an average of 7.6 unnecessary antibiotic doses, and cost savings upwards of USD 1000 per patient [21]. The standardization of treatment to a protocol that has been shown to lead to better outcomes and decreased costs for patients can ensure that all extremity GSW patients are afforded the appropriate prophylactic care to reasonably control infection risk. In order to expand the reach of this protocol, steps should be taken to increase the adherence internally and to encourage external trauma centers to adopt the same or similar guidelines.

In summary, trauma centers are seeing a high prevalence of extremity GSW injuries due to rising gun violence in the U.S., without standardized management practices to guide antibiotic prophylactic use and debridement decisions. The current research demonstrates that establishing guidelines for using single-dose cephalosporin antibiotics and a clinical follow-up for simple extremity GSWs can standardize care, save on resources, and minimize costs without compromising infection outcomes.

5. Conclusions

Civilian GSWs that affect the extremities are common, with the incidence of firearm violence increasing significantly in recent years. There is not a standardized protocol guid-

ing prophylactic antibiotic choice and management for extremity GSWs, leading to large variations in antibiotic use, operative management, and dispositions of extremity GSW patients. As these injuries increase in frequency, trauma centers should establish a treatment protocol among all services that involve managing patients with GSWs, including emergency physicians, trauma teams, and orthopedic surgeons. A single-dose first-generation cephalosporin antibiotic protocol in the emergency room is effective in minimizing the risk of infection for civilian extremity GSWs. We have demonstrated herein that initiating this protocol can be effective in promoting adherence to the protocol. Therefore, it would be both beneficial and feasible for more trauma centers in the U.S. to implement similar protocols for the treatment of civilian low-velocity GSWs to an extremity.

Author Contributions: M.P.N., H.A.V. and I.R.F. were involved in conception or design of the project. S.R.B., I.R.F., S.T.D., S.V. and M.A.S. were involved in the collection, analysis, or interpretation of data. S.R.B., I.R.F. and M.P.N. were involved in the drafting of the manuscript and revisions of intellectual content. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee) of HealthPartners Institute (A22-142, Approved on 2 August 2022).

Informed Consent Statement: Due to the retrospective nature of this study, informed consent of the patients was not required because the study analyzed de-identified clinical data of the patients.

Data Availability Statement: Data are contained within the article.

Conflicts of Interest: Mai P. Nguyen is a paid lecturer/consultant for AO North America, committee/board member for the Orthopaedic Trauma Association, and was awarded the OTA Resident Grant. The other authors certify that there are no funding or commercial associations that might post a conflict of interest in connection with the submitted article related to the author or any immediate family members.

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