Blisters Associated With Lower-Extremity Fracture: Results of a Prospective Treatment Protocol

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Objectives: To evaluate patient outcomes after treatment of lower-extremity fractures associated with blister formation and to assess complications after soft-tissue treatment using a prospective protocol.

Design: Retrospective evaluation of prospectively collected data.

Setting: Level I trauma center.

Patients/Participants: Between September 1999 and September 2003, 47 patients who had sustained a closed lower-extremity fracture with early development of fracture blisters in the zone of injury were followed. Blisters were characterized as either avoidable or unavoidable with respect to surgical incisions, and characteristics such as number, size, blood filled or clear filled, and the presence of an intact roof were documented.

Intervention: All blisters were unroofed, and antibiotic cream (silver sulfadiazine, Silvadene, King Pharmaceuticals Inc.) was applied twice daily until the blister bed had re-epithelialized.

Main Outcome Measurements: Fracture union and the development of wound or skin complications. Patient satisfaction with the cosmetic outcome of the treatment regimen was assessed through telephone survey at 23-month minimum follow-up.

Results: Twenty-eight patients presented with a single blister, and 19 had multiple blisters. Blister size averaged 9.7 cm^2. Twenty-two patients had blood-filled blisters, 20 had clear-filled blisters, and five had a combination of the two. Fracture patterns included 17 ankle fractures (OTA 44), 13 tibial plateau fractures (OTA 41), five tibial-shaft fractures (OTA 42), eight calcaneus fractures (OTA 45), and four pilon fractures (OTA 43). Mean delay in definitive surgical care was 7.7 days (range 0 to 20 days). The average delay of surgery for ankle fractures was 6 days (range 0 to 18 days), which was significantly less than the delay for calcaneus fractures (12 days, range 4 to 19 days, $P < 0.02$) and tibial plateau fractures (11 days, range 0 to 20 days, $P < 0.02$). Thirty-seven of the 45 patients (82.3%) available for follow-up at a mean of 27 weeks (range 14 to 35) had an uncomplicated postoperative course, and fracture union was achieved in 43 of 45 cases (95.6%). The soft-tissue complication rate associated with the standardized treatment regimen was 13.3% (6/45 cases), with three cases of minor soft-tissue breakdown, one superficial infection, and two major complications directly related to the presence of fracture blisters. Both major complications involved full-thickness skin breakdown occurring directly at the base of fracture blisters in patients with diabetes. The skin breakdown required further surgery in both cases. Including the two patients who developed nonunion, the overall complication rate for the treatment cohort was 17.7% (8/45 cases). At a mean follow-up of 51.9 months (range 23 to 73), three patients in the cohort had expired. Of the 42 patients available for evaluation, 28 patients (67%) were reachable for a telephone survey to assess satisfaction with the outcome of the fracture and soft-tissue management. Patients rated their satisfaction with the cosmetic appearance of their lower extremities after the standardized treatment regimen on a scale of 1 to 10 (with 10 representing very satisfied), with a mean of 9.07 (range 5 to 10). Six patients reported scarring at the sites of previous fracture blisters, all of which occurred after blistering of the blood-filled subtype. The presence of scarring significantly decreased patient satisfaction with cosmesis and overall treatment ($P < 0.0001$ and $P < 0.01$, respectively).

Conclusions: Treatment of fracture blisters with a silver sulfadiazine (Silvadene) regimen proved to be successful in minimizing soft-tissue complications by promoting re-epithelialization in all nondiabetic patients. At long-term follow-up, patients were generally satisfied with the cosmetic outcome of the treatment regimen. Postoperative scarring, which was more common with blood-filled blisters, significantly impacted patient satisfaction. We urge caution when planning to make a surgical incision around an area of both full-thickness (blood-filled) and partial-thickness (clear-filled) fracture blisters in diabetic patients because the zone of injury might extend beyond the borders of the fracture blister.

Key Words: fracture blisters, treatment, silvadene, outcome

(*J Orthop Trauma* 2006;20:618–622)

INTRODUCTION

Fractures complicated by the development of overlying blisters remain a clinical dilemma in orthopedics.[1–3] Currently, there is no universal consensus on the appropriate treatment of this associated soft-tissue injury when treating the underlying fracture. Additionally, little is known about the prognosis associated with the formation of fracture blisters in regard to soft-tissue healing or the risk of infection.[1–4] Much of this uncertainty is related to the paucity of scientific investigation into this clinical problem.

It has been hypothesized that a major factor in fracture blister development is injury to the dermal–epidermal junction resulting from high shear in the skin during the mechanism of

Accepted for publication August 22, 2006.

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fracture.[4,5] Two main subtypes of fracture blister have been identified (clear-filled and blood-filled), differing in the extent of dermal–epidermal separation after injury (Fig. 1).[2,3,5] Recommendations regarding surgical management of fractures in the presence of clear- and blood-filled blisters have ranged from incisions through the blistered region to surgical delay until re-epithelialization has occurred.[1]

The purpose of the current investigation was to prospectively follow a cohort of patients with a compromised soft-tissue envelope through their treatment course, using a standardized protocol for the management of fracture-associated blisters. We hypothesized that the standardized treatment protocol, which included deroofing blisters associated with lower-extremity fractures under Betadine preparation and application of silver sulfadiazine (Silvadene), would lead to successful blister-bed healing with a low complication rate and cosmetic results that would be acceptable to the study patients.

PATIENTS AND METHODS

During a 48-month period, the authors instituted a standardized treatment algorithm for the management of blisters associated with acute lower-extremity fractures presenting to one hospital within our system. Forty-seven consecutive patients who had sustained isolated or multiple, closed lower-extremity fractures associated with early development of fracture blisters in the zone of injury were prospectively followed to assess fracture and soft-tissue healing. Initially, all fractures were either closed-reduced and immobilized in plaster splints, or bridged in an external fixator and classified according to the OTA system.[6]

On presentation, each patient's soft tissues were evaluated by the on-call orthopedic surgery resident for the presence of blisters and abrasions, with documentation of the number, location, size, and consistency (clear filled versus blood filled) of associated fracture blisters.[2] Blisters were characterized as either avoidable or unavoidable with respect to planned surgical incisions. After povidone–iodine prep, each blister was unroofed by the orthopedic resident by sharply removing the overlying epithelium of the fracture blister with a sterile suture scissor at the blister's junction with the surrounding intact skin. Once the blister was unroofed and the edges were trimmed to the point of healthy tissue, silver sulfadiazine (Silvadene, King Pharmaceuticals Inc., Bristol, TN) was applied to the exposed blister bed and covered with a clean, dry 4 × 4 gauze pad and wrapped with an Ace bandage. If the patient was admitted for further management, Silvadene was applied to the blister bed twice daily with associated clean, dry dressing changes and the affected extremity elevated. Daily assessment of the blister sites were made and documented. Patients discharged home were given a prescription for Silvadene and detailed instructions regarding twice-daily application and dressing changes.

Forty-five of 47 patients underwent open reduction and internal fixation using plate and screws or interlocking nails. One patient was managed nonoperatively, and one patient was transferred to care at an outside institution. Timing of surgery depended on the resolution of soft-tissue edema and blister-bed re-epithelialization. Extremities were deemed operable when skin wrinkles were visible on the overlying skin of the injured extremity. The average delay of surgery directly attributable to the presence of blisters after the resolution of edema for each fracture was documented. When possible, surgical incisions were planned to avoid the blister beds. Perioperative antibiotics (first-generation cephalosporin) were given routinely to all patients.

After surgery, all blister beds continued to be treated with twice-daily Silvadene application and dry, clean dressings.

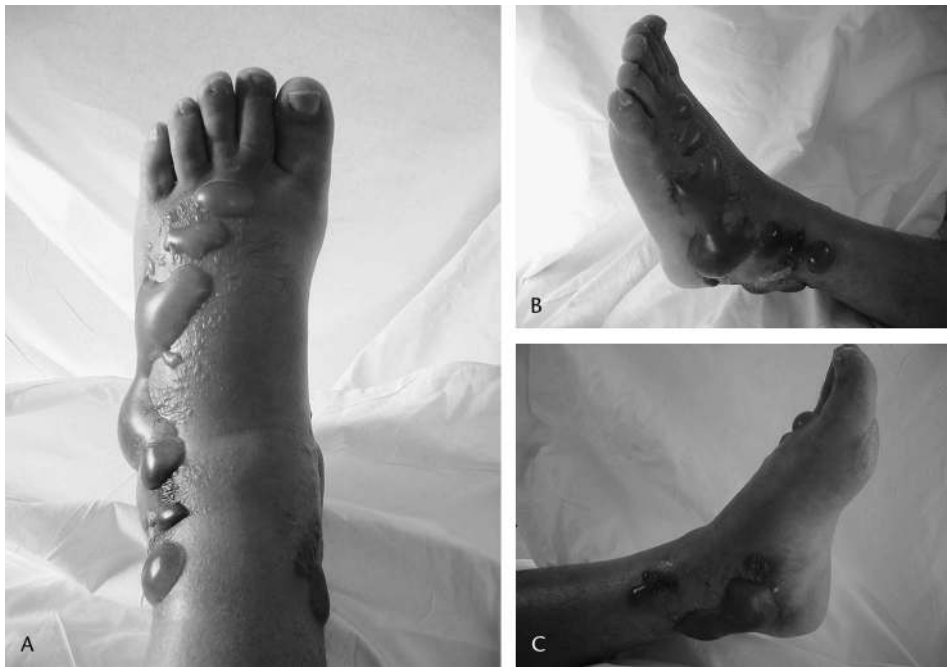

FIGURE 1. Clinical pictures demonstrating blisters associated with lower-extremity fracture. The patient was a 36-year-old male who sustained a trimalleolar ankle fracture during a motor vehicle accident. Surgical fixation of the fracture was performed 10 days after the injury (a surgical delay of 6 days secondary to the presence of the fracture blisters). Both clear-filled and blood-filled blisters are shown; the two types differ by the depth and extent of the injury to the dermal–epidermal junction.

Patients continued blister-bed treatment until the fracture blister had healed completely. Re-epithelialization was considered clinically complete when a moist dermal layer or granulation-type tissue was covered by an epithelial layer and the blister bed was no longer sensitive to touch. At follow-up, patients were monitored for evidence of fracture healing, wound or skin complications, or infection.

A follow-up telephone survey was performed to determine long-term outcome of the standardized treatment regimen. The survey focused on residual pain in the region of the previous fracture and fracture blisters, presence of scarring, satisfaction with the cosmetic outcome of the treatment regimen, and overall satisfaction with the patient's treatment course.

STATISTICAL ANALYSIS

The data were analyzed to determine the incidence of wound or skin complication and association between blister number, location, size and type, delay in definitive surgical care, and need for further surgery. Analyses were performed using a chi-square test and an unpaired Student's *t*-test. Statistical significance was defined as $P < 0.05$.

RESULTS

During the 4-year observation period, 655 patients who had sustained isolated or multiple lower-extremity trauma presented to our institution, of whom 47 developed fracture blisters in the zone of injury (incidence of 7.2%). Overall, there were 173 ankle fractures (OTA 44), 167 tibial-shaft fractures (OTA 42), 130 femur fractures (OTA 32), 110 tibial-plateau fractures (OTA 41), 38 calcaneus fractures (OTA 45), and 37 pilon fractures (OTA 43). The fracture-blister patient cohort consisted of 33 males and 14 females with an average age of 56.1 years (range 29 to 89 years). The mechanism of injury was motor vehicle accident (6), fall (28), and pedestrian struck (13). Twenty-eight patients had a single blister, and 19 had multiple blisters (mean 1.85 blisters per patient). Among patients with multiple blisters, the average number of fracture blisters was three (range, two to eight). Twenty-two patients (47%) had blood-filled blisters, 20 (43%) had clear-filled blisters, and five (10%) had a combination of the two. Blister size averaged 9.72 cm^2 (range, 1 to 60 cm^2). Fracture patterns associated with blister formation in this patient cohort included 17 ankle fractures (relative incidence of 9.8%), 13 tibial-plateau fractures (relative incidence of 11.8%), five tibial-shaft fractures (relative incidence of 3.0%), eight calcaneus fractures (relative incidence of 21.1%), and four pilon fractures (relative incidence of 10.8%). Two patients were lost to follow-up, leaving 45 patients available for analysis.

The overall mean delay in definitive surgical care from the time of presentation in this patient cohort was 7.7 days (range 0 to 20 days). The mean delay of surgery for ankle fractures was 6 days (range 0 to 18 days), proximal and distal tibial-shaft fractures 3.5 days (range 0 to 9), pilon fractures 6.75 days (range 1 to 12), calcaneus fractures 12 days (range 4 to 19 days), and tibial-plateau fractures 11 days (range 0 to 20 days). The mean delay of surgery for ankle fractures was significantly less than that for both calcaneal and tibial-plateau fractures ($P < 0.02$ for both comparisons).

In the 19 patients with multiple fracture blisters, eight (42%) had blisters that were clear filled, nine (47%) had blisters that were blood filled, and two (11%) had a mixed variety. Fracture blisters associated with calcaneus fractures or tibial-plateau fractures were more likely to be blood filled (73%) than blisters related to ankle fracture (53%), but the difference failed to reach statistical significance ($P = 0.13$).

Thirty-seven of the 45 patients (82.3%) available for follow-up at a mean of 27 weeks (range 14 to 35) had an uncomplicated postoperative course. In two ankle-fracture patients, further blistering developed after surgery, with the new blisters that formed being the blood-filled subtype. Minor skin breakdown developed medially in three ankle-fracture cases, one of which occurred in the region of postoperative blistering. Two of these cases healed without further intervention, with the third healing uneventfully after wet-to-dry dressing changes. One superficial infection occurred in a calcaneus fracture patient and resolved after a course of intravenous antibiotics.

There were two major complications directly related to the presence of fracture blisters. One major complication followed an ankle fracture-dislocation in an elderly diabetic female, sustained in a fall with an associated blood-filled blister present medially. The patient was neurovascularly intact distally on presentation. Full-thickness skin breakdown, which occurred at the base of a blood-filled fracture blister 0.5 cm proximal to a surgical incision 5 days after surgery, led to deep infection and the need for eventual ankle fusion. A second ankle-fracture patient, a 38-year-old male with non–insulin-dependent diabetes who sustained his injury during a motor vehicle accident, had persistent medial-ankle skin breakdown in the area of a clear-filled blister, necessitating hardware removal. Cultures in this patient were negative, and after hardware removal and debridement, the skin breakdown healed without incident. In both cases, the area of breakdown occurred directly at the base of the fracture blisters, not at the surgical site.

Forty-three of 45 cases (95.6%) achieved uncomplicated fracture union. Two patients developed nonunion, one after a tibial plateau fracture and the second after an ankle fracture, both cases united after revision surgery.

At a mean follow-up of 51.9 months (range 23 to 73 months), three patients in the cohort had expired. Of the 42 patients available for evaluation, 28 patients (67%) were reachable for a telephone survey to assess satisfaction with the outcome of the fracture and soft-tissue management. At this follow-up time point, six patients (21%) reported scarring in the region of their previous fracture blister. All six patients who developed scarring had fracture blisters of the blood-filled subtype at presentation. The scars were smaller than 1 cm in diameter in five of the six patients, and no patient reported avoidance of wearing shorts or skirts because of the cosmetic appearance of their lower extremities (Fig. 2). Residual pain in the region of the previous fracture was reported on a scale of 1 to 10 (no pain to severe pain) with a mean of 1.7 (range 0 to 7). Residual pain in the region of the previous fracture blister was

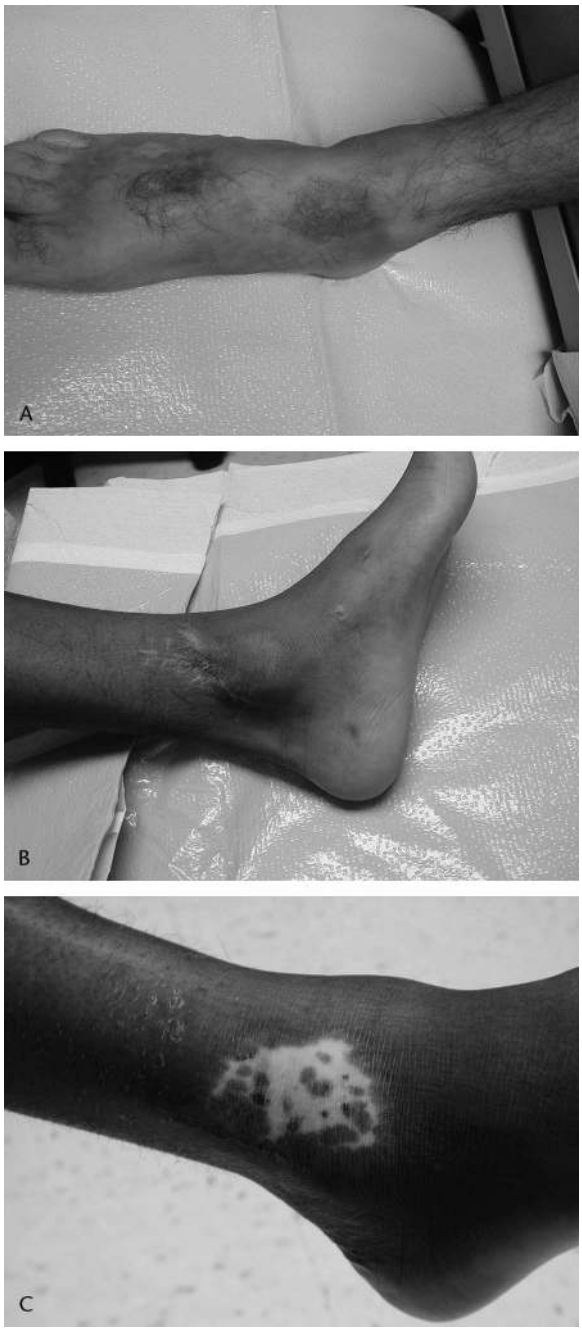

FIGURE 2. Clinical follow-up pictures demonstrating successful blister-bed healing after treatment with the standardized Silvadene protocol. A 40-year-old male sustained an ankle fracture during a fall, complicated by clear-filled blisters that developed on the dorsal and dorsolateral aspects of his foot and a blood-filled blister over the medial malleolus (A, B). As shown, the blister beds healed without significant scarring. Pigment loss occurred in two cases as demonstrated in panel C. This patient was a 52-year-old male who sustained an ankle fracture in a motor vehicle accident, complicated by the development of a large, blood-filled fracture blister over the lateral malleolus.

reported on a scale of 1 to 10 with a mean of 0.25 (range 0 to 2). Twenty-six of the 28 patients contacted (92.9%) were able to return to active employment. Patients rated their satisfaction with the cosmetic appearance of their lower extremities after the standardized treatment regimen on a scale of 1 to 10 (very dissatisfied to very satisfied) with a mean of 9.07 (range 5 to 10). Satisfaction with the overall treatment of the fracture and the fracture blisters was reported as a mean of 9.04 (range 5 to 10). The mean satisfaction rating for patients with posttreatment scarring was 6.16 (range 5 to 7) and 7.83 (range 7 to 9) for cosmesis and overall treatment, respectively, both significantly lower than that seen in patients without posttreatment scarring ($P < 0.0001$ and $P < 0.01$, respectively).

DISCUSSION

In the current study, fracture blisters, both clear filled and blood filled, were unroofed on presentation and treated with a topical antibiotic cream (Silvadene, King Pharmaceuticals Inc., Bristol, TN) and dry, clean dressings. Silvadene is a topical sulfonamide that acts as an inhibitor of bacterial folic acid synthesis. By preventing folate synthesis, Silvadene deprives bacterial cells of essential cofactors for purine, pyrimidine, and amino acid synthesis. We believe this protocol was successful in minimizing soft-tissue complications by promoting re-epithelialization while diminishing local bacterial counts in the blister bed. At a mean follow-up of 27 weeks, 37 of 45 (82.3%) had an uncomplicated postoperative course and healed without skin or wound complication. Of the five patients with skin breakdown, the two patients who did not heal with nonoperative management had diabetes mellitus as a comorbidity. Three of the five patients with postoperative skin complications had blood-filled blisters on presentation, with one developing new blood-filled blisters after surgery. On average, the presence of fracture blisters delayed surgical intervention for approximately 1 week, at the surgeon's discretion, with location of the fracture and associated blisters having a direct impact on the extent of delay. Postoperative scarring was more likely to occur in patients who had blood-filled blisters at the time of presentation. Additionally, the presence of postoperative scarring significantly impacted patient satisfaction with the cosmetic outcome of their treatment and with their overall management.

Reports concerning fracture blisters, their management, and outcome are limited in the orthopedic literature. In a clinical and histological study performed by Giordano et al,[2] skin biopsies were obtained from the edge of the surgical incision and the blister bed if incised through during the operative management of 13 ankle fractures. The authors identified two clinical types of fracture blisters, clear filled and blood filled. Histological evaluation demonstrated that both fracture-blister subtypes represented cleavage injuries at the dermal–epidermal junction. The main difference between the clear-filled and blood-filled blister types was the retention of some degree of epidermal cells in the clear-filled blisters, which the authors believed contributed to a faster re-epithelializaiton. The dermis of the blood-filled subtype was completely free of epidermal cells, which may have led to increased re-epithelialization time and its associated

morbidity. In this report, Giordano et al[2] describe uneventful healing of the incisions and blister beds in 12 of 13 cases in an average of 3 days, sealing off deeper structures. The single complication occurred in association with an incision through a blood-filled blister on the lateral aspect of the ankle, which healed with nonoperative treatment after 5 weeks. These results demonstrated no wound or skin complications when incisions were made through clear-filled blisters or when incisions were made adjacent to either blister type.[2]

Giordano and Koval[1] followed up this original case series with a prospective analysis of 53 cases of fracture blisters that included the 13 ankle fractures from the initial report.[1] In this study, no significant difference was found between the outcomes of various soft-tissue treatment techniques used, including aspiration, deroofing with Silvadene, or nonadherent dressing application and leaving the blister intact. At a mean follow-up of 3 months, 87% of patients re-epithelialized their blister beds without incident. The authors noted seven complications with blister-bed healing, all of which occurred in patients who presented with blood-filled blisters. Two of the seven occurred in patients whose incisions had been made through a blood-filled blister base. Six of the seven skin complications required split-thickness skin grafting for coverage. Based on their findings, the authors recommend leaving fracture blisters intact and only treating those that rupture spontaneously.[1] Our treatment regimen differed from the recommendations made by Giordano, with each fracture blister managed with sharp unroofing and the application of Silvadene. Although the overall incidence of complications was similar in our study, the soft-tissue complications that occurred in our patient population were much less severe, with no patient requiring skin grafting after skin breakdown.

Giordano et al[5] then followed up their clinical evaluation with a biomechanical study in which 60 cadaveric ankle-skin specimens were subjected to uniaxial strain to reproduce the dermal–epidermal injury proposed as the mechanism of fracture-blister formation.[5] They found that all specimens strained to 152% demonstrated complete separation of the dermis and epidermis, with scattered areas of retained epidermis on the dermis—a similar histologic picture to that of clinically observed clear-filled fracture blisters. Specimens strained to 167% demonstrated complete separation of the dermis and epidermis, which is analogous to the development of a blood-filled fracture blister. Based on their findings, the authors concluded that fracture blisters are caused by dermal–epidermal separation secondary to strains created in the skin during initial fracture deformation. When a critical strain is reached during the fracture mechanism, the differing elasticity and viscoelastic properties of the dermis and epidermis cause the layers to separate, with fluid filling the potential space as a result of the inflammatory cascade and starling forces from the vasculature.[5]

Varela et al[3] reported on 51 patients who developed fracture blisters 24 to 48 hours after injury. The presence of blisters affected patient management in 25% of cases, causing delays to surgical management and postoperative wound complications. Biopsy specimens were taken on 15 fracture blisters, with histologic evidence supporting the impression that fracture blisters are subepidermal vesicles. The fluid within the intact blister was found to be a sterile transudate, but on rupturing, the blister bed quickly became colonized with skin pathogens, with colonization continuing until re-epithelialization was complete.

Limitations of the current study include its retrospective design; a relatively small cohort population; heterogeneity in regard to fracture pattern, fracture mechanism, and associated blisters; and variable patient medical comorbidities. Additionally, because the current study is descriptive in nature, there was no control group for the purpose of making comparisons, a limitation that will be resolved with a future randomized controlled trial. Finally, it is important to acknowledge that the 14 patients who were unreachable for the follow-up portion of the investigation might represent a subpopulation with poor outcomes, which would adversely affect our reported results.

The current study was performed to evaluate patient outcomes after treatment of fractures in the face of fracture-blister formation and to assess complications after soft-tissue treatment with a prospective protocol. Unroofing clear-filled and blood-filled blisters and treating the blister beds with Silvadene was successful in minimizing wound and skin complications, with approximately 90% of the patients in our cohort healing without incident. Overall, patients were satisfied with the cosmetic outcome of the standardized treatment regimen. Although the presence of posttreatment scarring had no impact on the patients' functional capacity or choice of clothing, patient satisfaction with treatment was significantly impacted.

CONCLUSION

Our data demonstrated successful treatment of fracture blisters with a standardized Silvadene regimen, resulting in a cosmetic outcome with a high level of patient satisfaction. Our findings also indicate the impact of fracture blisters, especially on delay to surgical management. It is apparent from our data that blood blisters involve a higher risk of complications, presumably because they represent a more severe tissue disruption. The major complications reported in this investigation occurred in patients with comorbid diabetes mellitus.

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