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NEGATIVE PRESSURE WOUND THERAPY AND MEDICAL-GRADE HONEY COMBINATION SWIFTLY HEALS A LOWER EXTREMITY INJURY WITH BONE EXPOSURE IN A CAT

Alexandra PETEOACA[1], Niels A.J. CREMERS[2], Iuliana IONASCU[1], Andrei TANASE[1]

[1]University of Agronomic Sciences And Veterinary Medicine of Bucharest,
Faculty of Veterinary Medicine, 105 Splaiul Independentei, Bucharest, Romania
[2]Maastricht University Medical Centre, P. Debyelaan 25, 6229HX, Maastricht, Netherlands

Corresponding author email: alexandra_peteoaca@yahoo.com

Abstract

Lower extremity injuries in cats can present significant challenges by a lack of tissue, bone exposure, and bacterial contamination, requesting effective treatment methods. This case report describes the use of a combination of negative pressure wound therapy (NPWT) and medical-grade honey (MGH) dressing in the treatment of a complex lower extremity injury in a cat. An old injury in the metatarsal area of a 3-year-old male cat resulted in an open fracture of all the metatarsal bones. The wound was left open after osteosynthesis via intramedullary pin insertion. A combination of NPWT and MGH dressing was used to promote healing and prevent bacterial contamination. The combination of NPWT and MGH dressing was effective in promoting the healing and full closure of the soft tissue injury in this case. NPWT supported granulation tissue formation, maintained a moist wound environment, and prevented infection. The MGH dressing helped prevent further bacterial contamination and promoted wound healing. This case highlights the benefits of using a bimodal staged approach in the management of challenging lower extremity injuries in cats.

Key words: *negative pressure wound therapy, medical grade honey, lower extremity wound, secondary intention healing.*

INTRODUCTION

A significant portion of the recent literature on wound management discusses the challenges faced by veterinary practitioners in managing wounds, particularly those in the lower extremities that involve bone or tendon exposure and are highly contaminated (Erwin et al., 2021; Nolff, 2021). Effective wound management requires an understanding of the healing process and the use of appropriate techniques to promote healing. While many options are available, factors such as healing time, patient comfort, and cost must be considered. One critical period is the inflammatory phase until granulation tissue formation, during which removing necrotic tissue, controlling infection, and managing exudate are essential to promote healing. Negative pressure wound therapy (NPWT) is one technique that can be used during this period to target the post-wounding period and promote healing (Agarwal et al., 2019; Lee et al., 2009).

The use of suction devices or vacuum properties as an adjuvant in wound therapy has been quoted since antiquity and has been improved during the last century, leading to the development of NPWT technology in the past two decades (Miller, 2012). NPWT, also referred to as vacuum-assisted closure, involves the application of sub-atmospheric pressure to a wound. This is achieved through a closed system usually consisting of a porous foam, an adhesive drape used as a wound sealer, and intermittent or continuous vacuum applied through tubing connected to the foam via a small fenestration. Exudate control is provided as excess exudate is aspirated through the tubing into a canister, keeping the system entirely closed.

With increasing research results, the utilization of NPWT has expanded to a wider range of applications in human medicine (Seidel et al., 2020; Xie et al., 2010). In the veterinary field, the main focus has been on the open management of large contaminated or infected wounds, septic peritonitis, and skin graft augmentation (Stanley et al., 2013). Most studies have shown that NPWT results in reduced overall healing time, early granulation tissue formation, prevention of thermal and oncotic fluctuations, decreased edema, maintenance of optimal environmental conditions to keep the wound moist, three-dimensional wound contraction, modulation of wound healing mediators, increased tissue perfusion, and neovascularization (Ben-Amotz et al., 2007). While these properties have been proven in experimental settings on animal models such as rats or porcine models, the same results associated with small animals, particularly cats, are still under discussion and require further research (Jacobs et al., 2009; Morykwas et al., 2001). NPWT does not support epithelialization, thus the technique is limited to the stage when granulation tissue is formed (Demaria et al., 2011; Guille et al., 2007).

Medical grade honey (MGH) follows strict criteria to ensure the quality, safety, and efficacy of honey for medical applications (Hermanns et al., 2020). MGH has antimicrobial and wound healing activities, both are based on multiple mechanisms. The antimicrobial activities include acidic pH, osmotic activity, and the presence and formation of antimicrobial molecules make it effective against a broad-spectrum of microorganisms, without the risk of developing resistance (Pleeging et al., 2020). Wound healing is enhanced by creating a moist wound environment, its anti-inflammatory and anti-oxidative activities, and stimulation of autolytic debridement, angiogenesis, granulation tissue formation and reepithelialization (Smaropoulos et al., 2020; Pleeging et al., 2022a).

Once the wound bed transforms into healthy and well-vascularized tissue, there are two primary categories of wound closure options: secondary intention healing through the use of dressings and bandages, or surgical reconstruction via skin grafts or flaps. The market offers an immense range of dressings and topical products with evidence-based healing properties. However, choosing the right product or combination of products can be challenging due to several factors, including availability, price, previous experience, estimated time for healing, bandage change frequency, and individual factors. This case report highlights the successful combination of NPWT and MGH dressings for a lower extremity injury in a cat, demonstrating promising results.

MATERIALS AND METHODS

A 3-year-old, 3.2 kg intact male mixed-breed cat was presented to the University Veterinary Hospital of the Faculty of Veterinary Medicine of Bucharest with a one-week old open metatarsal fracture that was referred for limb amputation. The patient was normothermic, normotensive, and normopneic, with non-weight bearing lameness in the right hind limb. The surgical consultation revealed an open fracture in the metatarsal area with displacement and exposure of the fracture site. The patient is an outdoor cat, and the exact time of the traumatic event was unknown but estimated by the owner to be between 5-7 days prior to the examination. A limb-sparing approach was proposed, with intramedullary pin osteosynthesis of the fractured metatarsal bones, debridement, and secondary or tertiary intention healing of the wound. The initial surgery was performed by another surgical team, and the case was presented to the authors for wound healing. The initial wound evaluation was performed after surgery when intramedullary pinning was performed on the 2nd, 3rd, and 5th metatarsal bones of the right hind limb, and clinically nonviable tissue was surgically debrided. A deep wound affecting most of the anterior profile of the metatarsal area with bone and metal implant exposure, extensive muscle and tendon injuries, and severe tissue loss was observed. The perilesional tissue appeared viable at the initial evaluation, since surgical debridement had already been performed, and the wound was thoroughly irrigated with Ringer's lactate. A bacterial swab was taken for aerobic culture and antibiotic sensitivity testing. An aseptic technique was used to apply a bandage, which consisted of a MGH-based product (L-Mesitran Soft-gel, www.mesitran.com) as the contact layer, covered by sterile non-woven gauze pads, synthetic cast padding, and self-adhesive cohesive wrap. General intravenous antibiotics had already been initiated by the first surgical team and continued until the antibiotic sensitivity test results were available (clindamycin 10 mg/kg/day IV). Postoperative pain was managed by administering buprenorphine at a dose of 20 micrograms/kg every 8 hours for 5 days.

The decision was made to use a NPWT device. However, since the clinic did not have this equipment on-site, it took 48 hours to initiate the treatment. Due to the high exudation process, the initial bandage was changed twice more, as previously stated. The only difference was that the MGH gel was covered by a secondary dressing of polyurethane foam, which had a larger absorbent capacity to increase the interval between bandage changes. Within the first 24 hours, extensive oedema was noted in the perilesional tissue, with a colour change in the wound, which had a mostly ischemic aspect associated with areas of questionable viability (such as purple-dark-read muscle fibers and loose tendons). During pressure lavage (approximately 250 ml sterile buffered solution lactated Ringers using a pressure bag at 300 mm Hg) and bandage changes, no active haemorrhage was observed. Under sedation, the wound was irrigated with Ringer lactate and carefully dried using sterile gauze pads to prepare for the application of NPWT dressings. A silver-containing barrier dressing (Atrauman Ag 5 x 5 cm) was placed as the contact layer, and a fine-pored grey foam (VivanoMed Foam 10 x 7.5 x 3.3 cm) was precisely cut to fit the wound surface. The dressings were secured in place by two adhesive Hydrofilms that provided excellent impermeability and sealed the entire system. Due to the complex shape of the wound and its location on the lower extremity, a sandwich technique was employed to create an airtight environment by having the two Hydrofilms adhere to each other rather than to the perilesional skin.

To ensure proper functioning, the dressings were connected to a sterile canister and pump via port and plug connectors. A small window was carefully cut from the Hydrofilm covering the foam in the middle part to enable the port to contact the foam. The adhesive film covering the port was firmly sealed to maintain a closed environment and prevent any leaks.

Considering the bone exposure and the small size of the cat's paw, a continuous mode (VivanoTec Pro) with a pressure of -70 mm Hg was chosen for the NPWT system (Figure1). To prevent patient interference with the system, a covering bandage was applied using synthetic cast padding and a self-adhesive wrap.

The dressings were changed every three days for a total of three changes, allowing the NPWT to be used continuously for a period of nine days. The continuous vacuum was turned off only during bandage changes. During each dressing change, sterility was maintained, and new products were used to replace the entire system, with the only exception being the vacuum pump, which was reused.

At the conclusion of the NPWT treatment, healthy granulation tissue was observed, although moderate edema and exudative processes remained. To continue the wound healing process, a primary dressing of L-Mesitran foam, a polyurethane foam coated with a layer of MGH, was applied. To secure the dressing in place, a non-woven gauze pad and synthetic cast padding served as a secondary layer, with a self-adhesive cohesive wrap as an external layer, providing complete coverage of the lower extremity. Initially, the bandage was changed every two days, a total of three times, followed by every three days until day 49. Thereafter, the bandage was changed every 2-3 days, with L-Mesitran Soft Gel, a MGH gel, used as a contact layer, and the foam being replaced while keeping the additional layers consistent (Figure 2).

By day 61, the wound had fully healed, with continuous monitoring of limb mobility and pain since the initial injury involved metatarsal bone fractures. After the soft tissue had healed, a second surgery was performed to remove the metal implant, which was responsible for a small fistulous-like lesion with a tendency to reoccur. The cutaneous lesion was treated by applying a soft gel intralesionally. However, despite the formation of new epithelium, its integrity was compromised by the exudate produced due to the inflammatory process caused by the metal implant. At the end of the entire process (day 88), the animal had regained appropriate mobility and the limb was spared, with an extra rotation of the lower extremity.

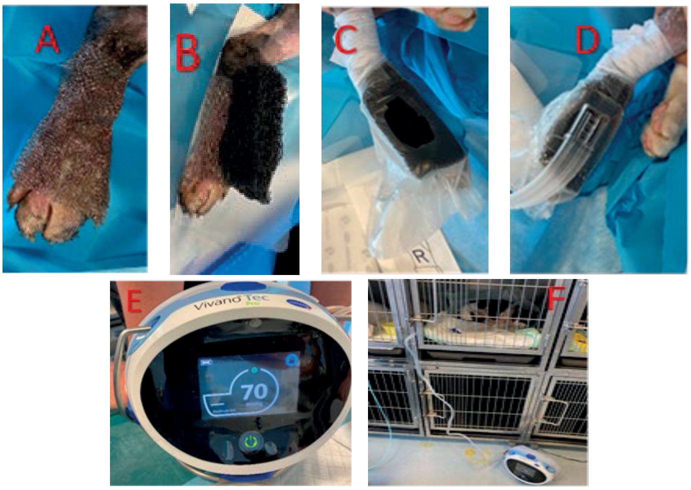

Figure 1. Negative pressure wound therapy dressing application

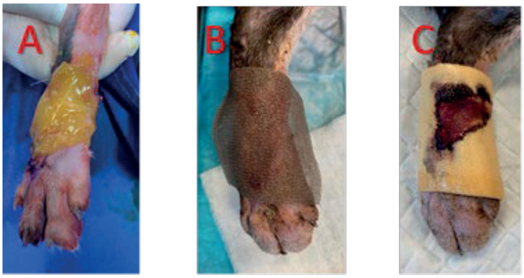

Figure 2. Dressings used for wound management
A. MGH gel; B. Silver dressing; C. MGH Foam

On day 5, the bacterial culture came back positive for *Enterococcus cecorum* and *Staphylococcus* spp., both of which were found to be resistant to Clindamycin, which had been prescribed previously. To address the bacterial infection, Clindamycin was discontinued and IV Ceftriaxone was initiated at a dose of 25 mg/kg twice daily for a total of 14 days. Throughout the entire wound healing process, the patient maintained a good appetite and did not exhibit any other symptoms. However, slight to moderate lameness was present when the cat used the bandaged limb. During the bandage change after the end of the NPWT, the cat did not require sedation and only exhibited minimal pain, which was associated with the bone lesion rather than the wound itself. No signs of pain were exhibited during wound lavage, cleaning, and redressing. After the initial course of opioid (Buprenorphine), no further targeted pain management was required. Additionally, for the first 5 days, a nonsteroidal anti-inflammatory drug (Meloxicam 0.2 mg/kg/day) was administered.

RESULTS AND DISCUSSIONS

Injuries to the lower extremities have been known to pose a challenge for small animals. When the severity of the wound is higher due to muscle, tendon, and bone injuries with bone exposure, the challenge is even greater.In addition, poor healing response in cats compared to dogs is a frequently mentioned aspect in research with exclusive feline patients, supported by specific studies such as those conducted by Bohling and his collaborators (Bohling et al., 2006; Bohling & Henderson, 2006). Furthermore, cats are more easily affected by stress and long hospitalization periods. Therefore, a method that would shorten the overall healing time, lower the manipulation frequency, and achieve good outcomes sounds promising. Although most case reports, case series, and comparative studies conducted on cats mention large skin defects, the severity of a wound has multiple factors of determination besides the extent of injury. The initial description of this wound makes it a good candidate for NPWT. The clinical aspect of the wound is presented in Figure 3.

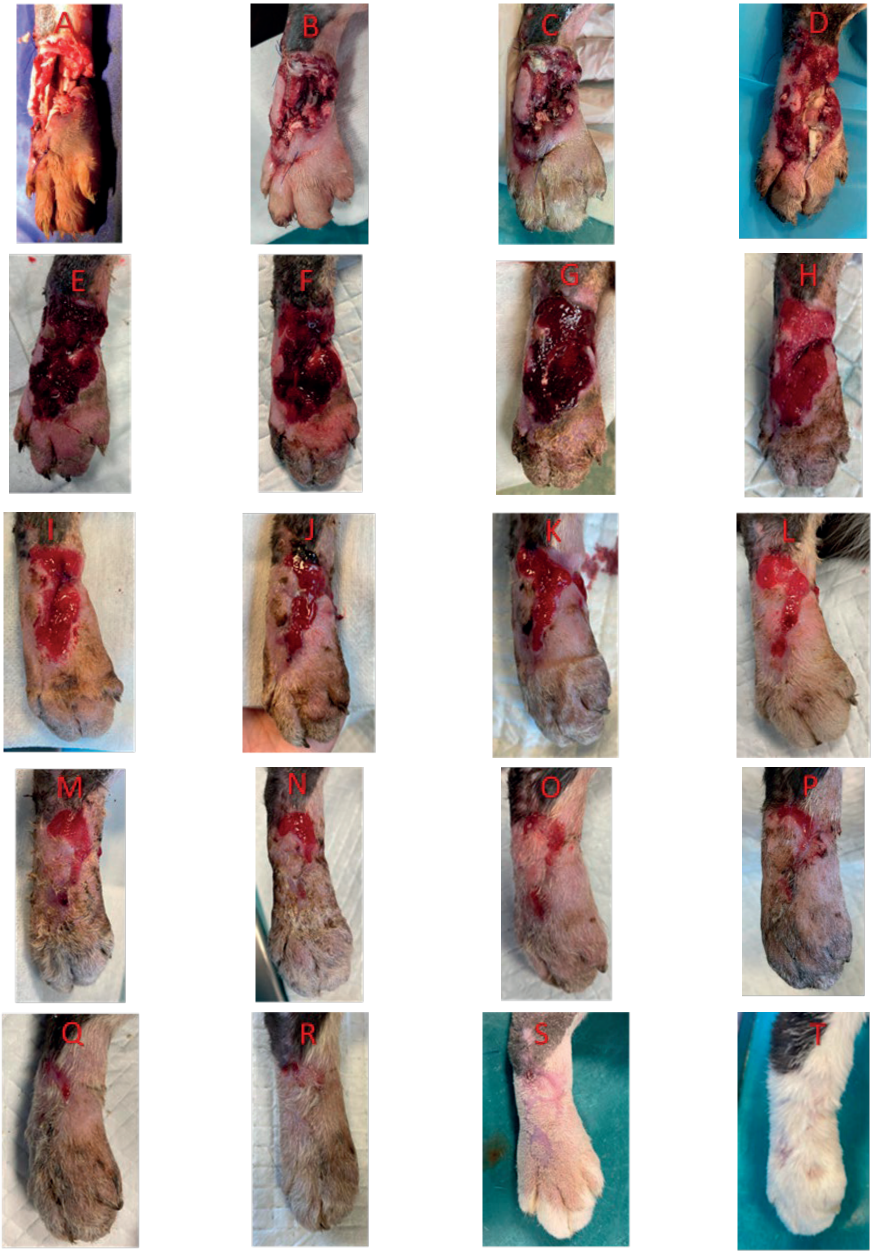

Figure 3. Wound healing timeline.
A. Day 1; B. Day 2; C. Day 4; D. Day 7; E. Day 10; F. Day 13; G. Day 16; H. Day 18; I. Day 21; J. Day 24; K. Day 27; L. Day 34; M. Day 40; N. Day 46; O. Day 50; P. Day 53; Q. Day 58; R. Full closure on Day 61; S. Follow-up on Day 74; T. Follow-up on Day 100.
Figure A-D: treatment with NPWT+ MGH, Figure E-R: only MGH treatment

At the conclusion of the NPWT, granulation tissue had covered almost the entire wound, reaching the skin level except for the central area. Although some edema was still present, it was significantly reduced compared to the initial presentation. The level of exudate also decreased, as depicted in Figure 4, which shows a clear difference between day 3 and day 13. The first image shows the foam dressing fully soaked with wound exudate after 12 hours, whereas the second image shows only partial saturation of the foam dressing with exudate after 48 hours.

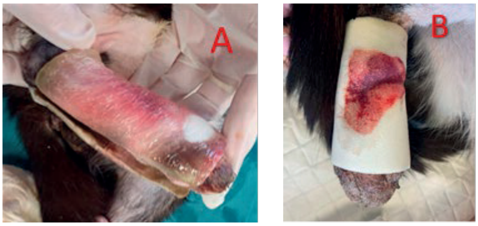

Figure 4. Exudate level. A. Day 2; B. Day 15

The main effect of the NPWT in this situation is the formation of granulation tissue, which is critical for the healing process as it covers the wound bed with healthy tissue. The increased perfusion facilitated by NPWT also plays a significant role in infection control by enhancing antibiotic delivery. Although the systemic antibiotics given are primarily responsible for infection control, previous research has suggested that the effect is potentiated by NPWT through various mechanisms. NPWT and MGH offer advantages over antibiotics, such as avoiding resistance, penetrating biofilms, and localized application. This aligns with the concept of antibiotics stewardship, aiming to reduce antibiotic use. Non-invasive or minimally invasive alternatives in wound management, like NPWT and MGH, can help achieve this goal. However, it's important to consider limitations such as the need for specialized equipment with NPWT and potential limitations of MGH against drug-resistant bacteria or severe infections requiring systemic treatment. Emphasizing the direction towards reducing antibiotic use through alternative products and systems is crucial. The dressings used in this case were according to the manufacturer's recommendations. The use of a non-adherent silver-containing barrier dressing is an additional layer not described in other protocols, justified by its ability to prevent maceration and adherence. The efficacy of silver ion-based dressings, known as antimicrobials is controversial, but when used in combination with vacuum-assisted closure as a primary layer, it has shown promising outcomes (Leaper, 2011; 2012). While using continuous vacuum for prolonged periods, granulation tissue may grow or become drawn into the grey foam, causing pain when removed and leading to minor setbacks when the tissue is disrupted during bandage changes. In this case, this aspect was observed during the last bandage change when the granulation tissue also developed a purple-dark red color. This color change may be associated with the high negative pressure used, but since the value was already considerably lower than pressure values in other studies, it was left unchanged.

Many publications provide guidelines for the duration and pressure values used in NPWT. However, there is still no consensus regarding the optimal parameters for different species, body locations, and specific characteristics. In this case, a value of -70 mm Hg was used, as advised by the manufacturer who had previous experience just with human subjects, taking into consideration the bone exposure and the small diameter of the lower extremity. The use of -70 mm Hg led to satisfactory results in promoting granulation tissue formation and controlling the infection after three dressing changes. These outcomes are consistent with previous literature and highlight the importance of individualizing treatment based on the patient's needs and response to therapy. Two approaches are available for lower extremity injuries after obtaining granulation tissue: skin grafting and secondary intention healing. The decision depends on factors such as the wound's extent and depth, presence of infection or inflammation, and patient's health. Skin grafting is preferred for faster and complete closure, but it is costly and invasive compared to secondary intention healing, which allows natural wound healing. In this case, secondary intention healing was chosen due to incomplete granulation tissue coverage, metatarsal instability, and potential complications with skin grafting caused by inflammation and exudate production.

The use of MGH products in wound management is a well-established practice, supported by ample research in both human and veterinary medicine, demonstrating the positive effects of MGH dressings on acute and chronic wounds (Aziz & Abdul Rasool Hassan, 2017; Lukanc et al., 2018; Mandel et al., 2019; Peteoaca et al., 2019; Pleeging et al., 2022a; Pleeging et al., 2022b; Vogt et al., 2021; Yilmaz & Aygin, 2020). Studies have reported that combining MGH with vitamins C and E, such as in L-Mesitran Soft, offers higher antimicrobial activity (Bocoum et al., 2023; Nair et al., 2020; Smaropoulos & Cremers, 2020). However, in highly exudative wounds, MGH alone may not meet all requirements for an ideal healing environment. While MGH is known to draw fluid out and reduce edema as a hyperosmotic product, it does not provide the best absorbent properties.

Polyurethane foam dressings are a good option for managing large amounts of exudate. Commercially available products come in a variety of combinations, such as silicon and hydrogel layers or adhesive margins covered by hydrofilms. One newer option is polyurethane foam coated with a MGH gel, such as L-Mesitran Foam (Mthanti et al., 2022). This product provides the benefits of MGH's healing properties while offering an absorbent layer that can maintain an optimal moisture level. Moist wound therapy is currently the main direction of wound healing guidelines. Using foam dressings reduces the frequency of bandage changes and provides a pain-free removal experience with no disruption of granulation tissue.

Combining L-Mesitran Soft gel with L-Mesitran Foam can be an adequate option for various types of wounds depending on the healing phase and wound characteristics. By preserving the antimicrobial and neovascularization-promoting properties of MGH and offering proper exudate control, this combination provides a competitive dressing. Additionally, having a versatile product line like this can significantly lower the number of dressing types needed in stock, providing a great advantage.

To achieve a more accurate assessment of the wound size at specific time points, the ImageJ analyzer software was utilized (Schneider et al., 2012). The measurements were calibrated using different markers in the image, and the area of the wound was calculated by tracking its contour. Although the wounds were measured in triplicates, it should be noted that small errors may be associated with the wound contouring performed by the human user. Furthermore, the three-dimensional aspect of the wound, such as its depth, was not taken into account, which may have introduced some bias in the measurements.

To obtain a more comprehensive evaluation of the wound healing process, consideration of other factors beyond the wound area, such as granulation tissue formation rate and quality, control of infection, exudate level, and other factors that may be more difficult to quantify, is essential. This approach could yield a more accurate overall healing score. Nonetheless, even without a depth correction factor, a visible decrease in the wound area was observed during the treatment until it achieved full closure. The results presented in Table 1 indicate that after 16 days, the wound size had reduced by almost half of its initial size and remained under one-quarter of its original size at day 34 (18%).

Table 1. Wound surface area corelated with the healing timeline

Day (healing timeline)	Area in cm	Percentage from initial area	Treatment
Day 1	4.274		Before NPWT
Day 4	4.978	100%	Start of NPWT
Day 7	4.305	86.48%	-
Day 10	3.518	70.67%	-
Day 13	3.467	69.646%	End of NPWT
Day 16	2.773	55.70%	MGH
Day 21	2.015	40.47%	MGH
Day 34	0.914	18.36%	MGH
Day 46	0.638	12.81%	MGH
Day 53	0.259	5.20%	MGH
Day 58	0.032	0.642%	MGH
Day 61	0.001	0.0200%	Healing complete

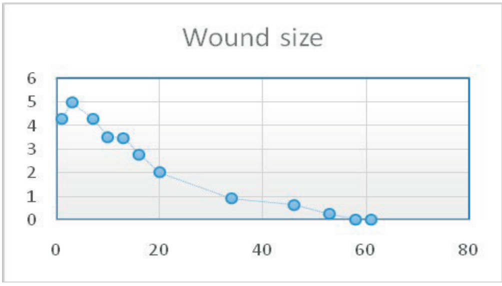

Figure 5. Wound size in cm^2 correlated to the healing timeline

These results are comparable to other similar cases and are considered satisfactory (Fehr et al., 2015; Nolff & Meyer-Lindenberg, 2014; Nolff et al., 2015; 2016; Pitt & Stanley, 2014).

At the one-year follow-up, a subtle scar was observed without any recurrence. The scar was mostly covered by hair, but there was a reduced range of motion in the metatarsal-phalangeal joint with a slight external rotation of the lower extremity. This case report cannot prove the superiority of the techniques used, but the results presented are consistent with recent literature regarding its efficacy.

Clinical studies on spontaneous injuries, rather than experimental wounding, present many biases and challenges in standardization. These challenges include unique patient characteristics, etiology, adjunctive treatments (such as orthopedic repairs, systemic antibiotics, medication for concurrent pathologies), the presence of infection and the type of pathogen present, time passed since the wounding, previous treatments, wound location, animal temper, species, and many others.

Although the standard of care often dictates surgical reconstruction as the optimal closure after healthy tissue formation, it is not always the best route for all patients, as previously presented. Open wound management remains a good alternative if an optimal healing environment is provided via interactive wound dressings.

CONCLUSIONS

Injuries to small animals' lower extremities with bone exposure pose a challenge, especially for cats, which have a poor healing response and are easily stressed by long hospital stays. NPWT can reduce healing time and manipulation frequency, as demonstrated in this case study. NPWT promotes granulation tissue formation and controls infection, although the optimal parameters for different species, body locations, and specific characteristics are not yet clear. The decision to use skin grafting or secondary intention healing after obtaining granulation tissue depends on the wound's extent, depth, the patient's health, and costs. MGH products and polyurethane foam dressings are viable options for wound management, and combining them may offer better outcomes. The use of NPWT and MGH may be an adequate protocol for challenging wounds, such as the one presented in this case report.

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