Abstract: Outpatient wound care centers are encountering patients with more complex wounds and an increased incidence of concomitant complicating comorbidities. As the population ages, patients with chronic wounds are presenting with multiple active disease processes that cause initiation of the wounds, impede wound healing, and preclude safely proceeding with surgical procedures, under anesthesia, to treat those wounds. Methods. Four warfarin-anticoagulated patients presented with large, full-thickness, necrotic, lower extremity wounds induced by hematomas from blunt trauma. Two of the wounds underwent scalpel debridement under local anesthesia while continuing anticoagulation. Following brief initial wound care with normal saline wet-to-moist dressing changes, continuous negative pressure therapy at 125 mmHg was initiated and continued for all wounds until the expansive tissue defects were decreased for 23.8 ± 3.2 days. All wounds were treated with application of a living bilayered skin substitute (LSS) in an outpatient setting while maintaining therapeutic anticoagulation. Results. All wounds completely epithelialized (100% closure) by 39.0 ± 21.9 weeks. One wound was completely relieved of its deep tissue defect to total epithelialization with one application of LSS. The largest wound (21.0 cm x 14.5 cm x 2.8 cm) with the greatest undermining (5 cm) was relieved of its tissue defect with a combination of negative pressure therapy and three applications of the LSS. The second largest wound (8.6 cm x 24.0 cm x 2.1 cm), which had an exposed knee joint capsule, required two applications of LSS. These results indicate that patients with large, full-thickness, necrotic, lower extremity wounds caused by traumatic hematomas while on anticoagulation therapy, can be appropriately managed as outpatients with aggressive sharp debridement under local anesthesia, negative pressure therapy for relief of the tissue defect, and bilayered skin substitute application to induce epithelial coverage. Conclusion. This approach eliminates the need for cessation of anticoagulation therapy and the use of more complex surgical procedures, such as myocutaneous flaps and skin grafts in patients with multiple underlying comorbid conditions.
Outpatient wound care centers are encountering patients with more complex wounds and an increased incidence of concomitant complicating comorbidities. As the population ages, patients with chronic wounds are presenting with multiple active disease processes that cause initiation of the wounds, impede wound healing, and preclude safely proceeding with surgical procedures, under anesthesia, to treat those wounds. Furthermore, the medications required to treat those disease processes often contribute to the development of those wounds, impair healing, and further complicate management.

Warfarin, a vitamin K antagonist and anticoagulant, is one such medication that is encountered with increasing frequency within the chronic wound care patient population. Common disorders such as chronic atrial fibrillation, venous thromboembolism, peripheral vascular disease, cardiomyopathy, recurrent transient ischemic attacks, and ischemic cerebrovascular accidents often require treatment with warfarin anticoagulation therapy. Unfortunately, hemorrhagic complications of warfarin therapy are frequent and debilitating. Low impact and minor blunt trauma to the lower extremities sustained by patients treated with warfarin anticoagulation therapy might result in the development of substantial subcutaneous tissue hematomas. As the hematoma expands, pressure within may exceed the perfusion pressure of the dermal and subdermal capillaries leading to devascularization of the overlying skin and adjacent subcutaneous tissue. This can result in full-thickness necrosis of the skin and subcutaneous tissue leading to the development of a very complex chronic wound that is difficult to manage, particularly in a chronically debilitated elderly patient with multiple concomitant medical comorbidities. In addition, anticoagulation therapy may have to be reversed in order to safely debride and reconstruct the wound. The present study employed an outpatient protocol of advanced wound care to treat four patients with large, full-thickness, necrotic, lower extremity wounds induced by hematomas from blunt trauma while on warfarin anticoagulation therapy.

**Methods**

Four elderly patients (77.2 ± 12.7 years) presented with large, full-thickness, necrotic, lower extremity wounds. The wounds developed at the site of blunt trauma, which occurred (14.5 ± 8.2 days) prior to presentation and caused expansive hematomas while on therapeutic anticoagulation therapy with warfarin (Figure 2A). The two patients with the largest wounds underwent sharp excisional scalpel debridement as outpatients while continuing therapeutic anticoagulation therapy with warfarin. The two patients (cases 1 and 3) with the smallest wounds had undergone inpatient operative debridement under local anesthesia with sedation following cessation of anticoagulation therapy and near-normalization of the International Normalized Ratio (INR). Further treatment for both patients was continued on an outpatient basis while maintaining therapeutic anticoagulation therapy with warfarin. Following initial debridement, wound dimensions averaged 19.1 cm ± 8.9 cm in length, 12.2 cm ± 9.5 cm in width, and 2.5 cm ± 3 cm in depth with undermining. Following primary short treatment with wet-to-moist saline dressing changes, continuous negative pressure therapy (V.A.C.®, KCI, San Antonio, TX) was instituted at -125 mmHg and continued to all wounds until the expansive tissue defects were relieved for an average of 23.8 ± 3.2 days (Figures 1A, 2B, 3A, 4A). The wounds underwent periodic sharp debridement under local anesthetic, as needed, to remove any nonviable tissue and adherent fibrinous exudate.

All wounds were then treated with application of a living bilayered skin substitute ([LSS], Apligraf®, Organogenesis, Canton, MA) in an outpatient setting, while maintaining therapeutic anticoagulation to facilitate wound epithelialization and closure (Figures 1B, 2C, 3B, 4B). All wounds underwent sharp excisional debridement prior to LSS application. The LSS was meshed with a 1.5:1 plate prior to placement and was secured to the wound beds.
with tacking absorbable 4-0 Vicryl sutures and covered with a nonadherent dressing (Mepitel®, Mölnlycke, Norcross, GA). A silver-impregnated antimicrobial dressing (Acticoat™, Smith & Nephew, Hull, UK) was placed over the nonadherent dressings, and multi-layered dry plain gauze dressings were then applied. Multiple layered compression dressings (Profore™, Smith & Nephew, Hull, UK) were then placed to control leg edema. Dressings were usually changed at weekly intervals, unless soiling or disruption necessitated a more frequent change. The wounds were not debrided for 6 weeks following application of the LSS. Additional LSS application was performed if, after

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CASE 2

Figure 2A. Week 1.

Figure 2B. Week 11, pre-LSS.

Figure 2C. Week 11, first LSS.

Figure 2D. Week 16.

Figure 2E. Week 32.

Figure 2F. 1-year follow up.
CASE 3

Figure 3A. Week 4.

Figure 3B. Week 6, LSS application.

Figure 3C. Week 7.

Figure 3D. Week 8.

Figure 3E. Week 10.

Figure 3F. Week 20.

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6 weeks following LSS application, further epithelialization and closure of the wounds stalled.

**Results**

All wounds completely epithelialized (100% closure) by an average of 39.0 ± 21.9 weeks from initiation of therapy. The wound in case 2 (8.6 cm x 24.0 cm x 2.1 cm), which demonstrated initial post debridement exposure of the knee joint capsule, required a second application of the LSS to facilitate closure. Two wounds (30.0 cm x 1.5 cm x 2.5 cm, 16.8 cm x 8.8 cm x 2.5 cm) were relieved of their tissue defect by inpatient operative debridement followed by a combination of negative pressure therapy then four and one applications of LSS, respectively (patients 1 and 3). The largest wound (21.0 cm x 14.5 cm x 2.8 cm) with the greatest undermining (5 cm) occurred in the oldest patient (90 years). It took more than twice as long to heal than any of the other three wounds (68 weeks) and required three applications of the LSS (case 4). This patient suffered from massive lower extremity

**Keypoints**

- All wounds completely epithelialized (100% closure) by 39.0 ± 21.9 weeks.
lymphedema that was eventually best controlled with daily use of a sequential gradient pump.

**Discussion**

Older adults who present with full-thickness, necrotic, lower extremity wounds caused by traumatic hematomas while on therapeutic anticoagulation therapy with warfarin are challenging to manage. The extent of tissue loss and associated wound defects, the concomitant comorbidities plaguing these patients, the need to maintain anticoagulation therapy, and the logistics of coordinating ongoing wound care led to the development of the efficacious protocol employed in these case studies.

It has been reported that approximately 6% of the population older than 65 years have the most common cardiac arrhythmia—atrial fibrillation. 4 The use of long-term antithrombotic therapy with anticoagulant agents, such as warfarin, reduces the relative risk of stroke from atrial fibrillation by approximately 65% and the cost effectiveness of anticoagulation therapy in older patients has been well validated. 5 Nonetheless, the bleeding complications associated with warfarin therapy can be life threatening, at worst, or quite debilitating as in the case of lower extremity hematomas caused by even mild blunt trauma. Continued intramuscular bleeding of the lower extremities has been described to progress to compartment syndrome in elderly patients following low-energy trauma while taking warfarin. 6 Deep dissecting hematoma of the lower extremity was previously described in 34 elderly patients with underlying dermatoporosis (chronic cutaneous insufficiency or fragility syndrome). 7 Fifty percent of the patients were treated with anticoagulation drugs at the time of injury that induced the hematomas. Skin necrosis developed as a late manifestation. Hospital treatment consisted mainly of deep incision and debridement followed by either direct closure, skin grafting, or secondary wound healing with a mean hospital stay of 3.5 weeks. This experience is in stark contrast to the authors’ near total outpatient protocol that was minimally disruptive to the patients’ routines, while maintaining anticoagulation therapy with warfarin.

Following the debridement of nonviable tissue from the necrotic wounds, we opted to proceed with negative pressure wound therapy (NPWT) to facilitate wound bed granulation and relief of the expansive tissue defects. While the exact mechanism of action of NPWT is uncertain, the authors’ experience is consistent with the scientific evidence that supports the use of NPWT to decrease bacterial burden, decrease edema and drainage, increase wound perfusion, increase granulation tissue formation, and stimulate wound contraction. 8

At cessation of NPWT, the wounds displayed a wide-open viable granulation bed. In order to maintain anticoagulation, eliminate the need for an operative procedure and its potential associated skin graft harvesting site complications, minimize patient discomfort, and risk of anesthetic and inconvenience, the authors opted to apply a LSS (Apligraf) to the wound beds to foster epithelial coverage and wound closure. Apligraf is composed of keratinocytes and fibroblasts cultured from newborn foreskin cells. It approximates human skin in structure and barrier function and contains matrix proteins and cytokines known to be integral to the wound healing process. In addition, it provides a dermal matrix to enhance cellular migration and to quench proteolytic enzymes. Randomized multicenter controlled trials have established the efficacy of Apligraf in healing refractory venous stasis ulcers and diabetic, neuropathic foot ulcers. 8–10

The described protocol allowed for treatment and closure of complex wounds in elderly patients with multiple comorbidities on warfarin anticoagulation therapy in a predominant outpatient setting. The protocol eliminated the need for an operative procedure under general or regional anesthesia, did not require cessation and subsequent reinitiation of anticoagulation therapy, did not necessitate creation of an additional wound created by harvesting skin in these dermatoporotic elderly patients, and eliminated the chance of failure of a split-thickness skin graft. Older age (> 55 years) has been previously cited as a significant adverse factor on the percentage take of split-thickness skin grafts. 11 One cannot argue that split-thickness skin grafting is the “gold standard” for wound coverage and closure in the vast majority of clinical settings. Unfortunately, the patients in this study were not appropriate candidates for that therapy at the time of initial debridement due to the expansive dimensions of their tissue defects. This was particularly the case in the patient with the exposed knee joint capsule. Negative pressure therapy was required for an average of more than 3 weeks to facilitate relief of the massive tissue defects. While expeditious wound closure is ideal, the patients in the present study did not experience any adverse sequelae, require hospitalization, or suffer significant disruption in lifestyle on the path to closure of their wounds.

The authors have adopted a protocol of placing a nanocrystalline silver dressing over a nonadherent dressing covering the bilayered skin substitute application site, which was derived from our initial experience with...
application of the bilayered skin substitute. Absence of the nanocrystalline dressing resulted in bilayered skin substitute application sites that were rich in malodorous drainage, overly colonized with deleterious bacteria, and too frequently plagued with cellulitis of the adjacent skin. While there have been in vitro studies that indicate the toxicity of nanocrystalline silver to human keratinocytes and fibroblasts, in vivo evidence is lacking. The authors’ experience with nanocrystalline silver supports its decrease in matrix metalloproteinase activity and reduction in wound exudate and bioburden levels. Patients experience less pain, require decreased frequency of dressing changes, and seem to have enhanced wound healing. The authors’ healing rates with the bilayered skin substitute using a nanocrystalline dressing have been comparable with the best results reported in the literature.

**Conclusion**

Patients with large, full-thickness, necrotic, lower extremity wounds caused by traumatic hematomas while on warfarin anticoagulation therapy can be appropriately managed as outpatients. Aggressive sharp excisional debridement under local anesthesia, negative pressure therapy for relief of the tissue defect, and application of a bilayered skin substitute to induce epithelial coverage and definitive wound closure proves to be an effective treatment protocol.

**References**