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Comparative Analysis of a Novel Multi-Tissue Platform (MTP) Powder in Lower Extremity Amputations

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Abstract

Background: Lower extremity amputations (LEAs) carry high rates of postoperative wound complications and reoperations, particularly among patients with significant comorbidities. Extracellular matrix (ECM) technologies have demonstrated promise in enhancing wound healing, and Multi-Tissue Platforms (MTPs) represent a newer generation of bioactive scaffolds designed to optimize tissue regeneration. This study evaluates the impact of an MTP-based wound powder (XCelliStem) on postoperative outcomes following below-knee (BKA) and above-knee (AKA) amputations.

Methods: A single-center retrospective analysis was conducted on 348 patients who underwent 449 major LEAs between January 2022 and September 2024. Forty-seven patients received XCelliStem powder during wound closure, while 301 patients (402 amputations) comprised the traditional cohort. Demographics, comorbidities, need for reoperation within six months, and requirements for local wound care were recorded. Application of XCelliStem was standardized across all cases.

Results: Reoperation occurred in 30.0% of the traditional cohort (94 BKAs; 27 AKAs) compared with 6.4% of the XCelliStem cohort (3 BKAs), representing a statistically significant reduction. The calculated number needed to treat (NNT) was 4.2, or 6.0 when excluding planned reoperations. Local wound care requirements did not differ significantly between groups (traditional: 19.6%; XCelliStem: 23%). No patient-selection bias or significant differences in comorbidity burden were identified between cohorts.

Conclusion: The use of an MTP-based ECM powder during LEA closure is associated with a significant reduction in reoperation rates, suggesting improved early wound healing outcomes. These findings support the incorporation of MTP technology as an adjunct to standard closure techniques. Further prospective studies are warranted to validate these results and evaluate outcomes within specific high-risk subgroups.

Keywords

Above-knee amputation, AKA, below-knee amputations, BKA, extracellular matrix, Lower extremity amputations, Multi-Tissue Platform, regenerative medicine, reoperation rates, wound healing, XcelliStem.

INTRODUCTION

Despite advancements in medical management, lower extremity amputations (LEA) remain a common surgical procedure performed worldwide for various causes. Excluding trauma, an estimated 150,000 lower-extremity amputations are performed annually in the United States [1]. Peripheral artery disease is the leading cause of LEAs, followed by atherosclerosis and diabetes mellitus. Patients undergoing LEAs often have multiple comorbidities that impair wound healing, including tobacco use, diabetes mellitus, and cardiovascular or renal disorders [2].

Below-knee amputation (BKA) and above-knee amputation (AKA) are associated with significant mortality rates, with some studies reporting a 5-year survival as low as 33% [2] [3] [4] [5]. Among these procedures, BKAs are more frequently associated with wound healing complications with a range in severity of complications from superficial skin breakdown requiring local wound care, to complete stump dehiscence, recurrent osteomyelitis, or progressive ischemic insults, all of which can lead to reoperation and either local stump revision or more proximal amputation [6].

LEAs are linked to substantial morbidity and mortality due to newly acquired physical limitations, increased metabolic demands, pre-existing comorbidities, and a decline in quality of life [7]. Perioperative complications are common and remain a challenge despite the implementation of surgical drains and closed-incision negative pressure wound therapy (NPWT). While these interventions have improved overall outcomes, wound complication rates have remained relatively unchanged [8].

Extracellular Matrices (ECM) have become widely used in

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surgical practice, demonstrating improved wound healing through full tissue incorporation [9], [10]. ECMs have gained significant popularity in the surgical world, particularly in reconstructive surgery, due to their wound-healing benefits [11], [12], [13]. ECMs are derived from decellularized tissue and serve as a scaffold to support host tissue regeneration [11] [12]. Initially, ECMs were believed to function solely as a structural framework, however, further research has revealed they also contain bioactive molecules such as collagen, elastin, laminin, fibronectin, sulfated glycosaminoglycans (sGAGs), lipids and growth factors [11]. Common donor tissues for ECMs include small intestine submucosa, urinary bladder, and dermis. Upon placement in an active wound, the host response to ECMs begins within hours, with mononuclear cells infiltrating the area to initiate a complex process of tissue remodeling and repair [11], [14], [15].

Advancements in regenerative medicine have introduced the concept of ECMs as Multi-Tissue Platforms (MTPs). MTPs are created using multiple donor tissues, each chosen to provide an optimized scaffold and blend of bioactive molecules and growth factors. These products have been shown to enhance wound healing, stimulate the body's inflammatory response, and are effective in infected wound beds [16]. Given the persistent challenges of wound complications and high reoperation rates associated with LEAs, this study examines the potential benefit of incorporating MTP-based wound powders during the closure of BKAs and AKA and their impact on rates of reoperation and wound complications.

Several ECM products are currently available on the market. XCelliStem was selected for this study as it is the only Multi-Tissue Platform commercially available. Additionally, it utilizes a balanced formulation of collagen to non-collagenous proteins, with a ratio of 55% protein to 45% collagen, compared to other products that contain up to 90% collagen. Seroma rates were found to increase four-fold with hydrolized collagen powder, whereas XCelliStem has been shown to significantly reduce seroma formation [11], [17].

METHODS

Our study utilized a single-center retrospective model to evaluate all patients who underwent major lower extremity amputations (BKA or AKA) at our institution between January 2022 and September 2024. Patient demographics, including age, gender, and co-morbidities were documented. In an effort to reduce wound complications and rates of reoperation following lower extremity amputations, several surgeons at our institution have incorporated a MTP ECM (XCelliStem Wound Powder, RTT, Orlando, FL) into their practice. This study was approved by the Spartanburg Regional Healthcare System Institutional Review Board (IRB #2244894).

A total of 348 patients who underwent either BKA or AKA were included in the study. There were no exclusions for pathophysiologic cause of amputation. Of these, 47 patients received XCelliStem during wound closure, while 301 patients did not and were classified as the "traditional" cohort. There was no selection bias between cohorts, and both had similar rates and severity of peripheral vascular disease, diabetes, soft tissue infection, and traumatic injury. Factors such as BMI, level of perfusion status, renal function, A1C and overall functional status were taken into account to determine level of amputation.

Postoperative outcomes, specifically the need for reoperation or local wound care were tracked. Local wound care was defined as any additional care required for the incision during the healing process, including management of incision line necrosis, superficial incisional breakdown, or dehiscence. These issues were addressed through treatment provided by the patient, home health services, or clinic nursing staff. Reoperation rates were defined as cases requiring a return to the operating room within six months of the initial procedure, either for stump revision or to perform a more proximal amputation.

XCelliStem was applied uniformly within the deep aspect of the amputation site and beneath the subcutaneous tissue layer before wound closure (Figure 1). The application process was standardized across all patients to ensure consistency.

Figure 1. Peri-operative application of XCelliStem Wound Powder in a uniform layer throughout the deep aspect of a below knee amputation

RESULTS

Between 2022 and 2024, a total of 449 lower extremity amputations were performed on 348 patients at a single institution by multiple surgeons. Of these cases, 47 utilized XCelliStem wound powder during closure while 402 did not. The procedures included 294 BKAs and 155 AKAs. Patient

demographics were recorded without exclusions based on age, race, gender, or coexisting comorbidities. Major comorbidities within the patient population included, but were not limited to diabetes mellitus, renal failure requiring dialysis, history of myocardial infarction, stroke, and peripheral arterial disease. The use of XCelliStem was not subject to specific patient selection or exclusion criteria; it was primarily determined by surgeon preference and product availability. There was no difference in pathophysiology or comorbidity rates between the study group and the control.

Reoperation rates and local wound care needs were tracked for both the traditional and XCelliStem cohorts. Planned reoperations, such as guillotine amputations, were included as reoperations within the traditional cohort, consistent with current literature. In the traditional cohort, 94 BKAs (35%) and 27 AKAs (20%) required reoperations, resulting in an overall operative revision rate of 30.0%. In the XCelliStem cohort, 27 BKAs and 20 AKAs were performed, with only 3 BKAs (6.4%) requiring reoperation (Table 1).

Table 1. Reoperation and local wound care rates of LEAs for both traditional and XCelliStem cohorts

Traditional	Total Cases	Reoperation	Wound Care
BKA	267	94 (35%)	57 (21%)
AKA	135	27 (20%)	22 (16%)
Total	402	121 (30%)	79 (20%)
XCelliStem	**Total Cases**	**Reoperation**	**Wound Care**
BKA	27	3 (11%)	7 (26%)
AKA	20	0 (0%)	4 (20%)
Total	47	3 (6.4%)	11 (23%)

A Chi-squared test confirmed that this difference was statistically significant for both BKAs as well as AKAs with p-values of 0.009 and 0.038 respectively. These findings suggest a statistically significant association between the use of XCelliStem during closure of lower extremity amputations and a reduction in reoperation rates. The overall number needed to treat (NNT) was calculated at 4.2, and if planned reoperations, such as guillotine amputations, were removed from the traditional cohort, the number needed to treat was 6.0.

Local wound care needs were also analyzed for both cohorts, with rates of 79 (19.6%) in the traditional cohort and 11 (23%) in the XCelliStem cohort. However, this difference was not statistically significant.

Conflicts of Interest

The authors declare no conflicts of interest related to this study. No financial support was provided for the study or to the authors by the manufacturer in any way.

Future Direction / Limitations

This study has shown the potential benefits of XCelliStem in the reduction of reoperation rates for LEA. This has led to a practice change among our surgical group to include XCelliStem in all LEA prior to closure. We plan to revisit this data set once sufficient data has been collected and expand our analysis to include BMI, renal function, A1C, vascular status, and other comorbidities that are known to affect healing rates.

DISCUSSION

Lower extremity amputations are associated with significant morbidity and mortality due to newfound physical limitations, increased metabolic demands, preexisting comorbidities, and a decreased quality of life. Perioperative complications have been reported in up to 40% of patients who undergo LEA, with 5-year mortality rates reported as low as 33%. While NPWT and surgical drains have improved outcomes, there has been minimal progress in reducing overall wound complications and reoperation rates.

Postoperative management of LEAs varies greatly. While our study includes the outcomes of multiple surgeons, they all utilize the same prosthetics company that manages postoperative care of the amputations in terms of edema management, stump shrinkers and placement of prosthetics. The group also has a shared clinic and wound care team that manages any local wound care on an individual basis depending on the patient's needs. Management of edema in the immediate postoperative setting was done with ACE wrap for the first two days. Once removed, the patients were managed on an individual basis to best optimize their recovery. This ranged from continued ACE wraps to lymphedema wraps, to casting with weekly assessments by a dedicated wound care team as well as evaluation by the prosthetics team to determine timing and application of a stump shrinker.

The discharge destination of our patients was variable, including skilled nursing facilities, acute care rehab facilities, or home with or without home health nursing. This variability was determined on a case-by-case basis and was heavily influenced by insurance status and patient preference. All patients were seen for follow up in our clinic for continued monitoring of stump healing.

CONCLUSION

MTPs are gaining popularity in surgery, particularly within reconstructive surgery, with data demonstrating improved outcomes and enhanced wound healing. This study evaluated the use of a MTP-based powder during the closure of LEAs. While future research should include a larger cohort and explore the use of MTPs in specific pathologies to determine whether improved outcomes can be achieved in specific populations, our data indicate a significant reduction in overall reoperation rates for LEAs with the use of MTPs during closure, as well as a low NNT.

These findings represent a promising advancement in the management of LEAs and highlight the potential of MTPs such as XCelliStem, in promoting wound healing. Based on our results, we advocate for the use of MTPs during LEA

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closure, as they have demonstrated a statistically significant reduction in the need for reoperations. This advancement has the potential to reduce healthcare costs by millions of dollars annually.

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