

Wound Healing in a Glottic Cancer Patient: A Case Report on Nutritional Intervention

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Abstract Background: Advanced glottic cancer often poses significant challenges in postoperative wound healing after total laryngectomy and radiation. **Case Presentation:** A 76-year-old male diagnosed with T3N0M0 glottic cancer experienced severe wound-healing complications, including a pharyngocutaneous fistula (PCF) and persistent wound dehiscence, after undergoing extensive surgery and radiation therapy. **Management and Outcome:** A tailored nutritional intervention involving arginine supplementation was introduced to support tissue repair for four weeks. Arginine was selected for its role in stimulating collagen synthesis and enhancing immune function. This approach resulted in substantial improvement in wound healing and overall recovery. **Discussion:** This case demonstrates the role of arginine supplementation in supporting wound healing and recovery in cancer patients after surgery and radiation. By enhancing collagen synthesis, immune function and tissue repair, arginine provides a targeted nutritional strategy for improving postoperative outcomes.

Key Words Glottic Cancer, Head and Neck Cancer, Wound Healing, Arginine, Oral Nutritional Supplementation (ONS), Enteral Feeding

INTRODUCTION

Head and neck cancer (HNC) includes malignancies of the oral cavity, pharynx, larynx and hypopharynx, accounting for over 4% of all cancer cases globally [1]. Treating HNC patients poses unique challenges, particularly the high prevalence of surgical site wound complications, which affect 19% to 29% of cases [2]. These complications can significantly impair recovery and quality of life. Treatment modalities such as surgery, chemotherapy and radiation therapy can significantly compromise vital structural functions, including breathing, speech and swallowing. This highlights the critical importance of effective wound healing in preserving these essential functions [3].

Nutritional deficits are a pervasive issue among cancer patients, with approximately 90% experiencing severe malnutrition [4]. This is particularly pronounced in 30-50% of HNC patients due to the tumor location and the intensity of treatment [1]. Patients with HNC commonly encounter common symptoms such as dysphagia, xerostomia, mucositis and altered taste perception, all of which impede adequate oral intake [5]. These complications impair tissue regeneration, increase infection risks and

delay recovery, emphasizing the need for targeted nutritional interventions beyond surgical care [6].

Addressing these nutritional deficiencies is crucial, as wound healing is a complex and metabolically demanding process requiring extensive cellular activity, particularly after surgical interventions [7]. Proper healing hinges on the availability of both macronutrients and micronutrients, including zinc, selenium and vitamins A, C and E [8]. Among these, arginine emerges as a critical nutrient due to its multifaceted role in supporting immune function [7]. Furthermore, arginine's anti-inflammatory properties and its role as a precursor for amino acids essential to tissue repair make it particularly beneficial for overcoming the nutritional challenges HNC patients face [8].

Tailored nutritional strategies, particularly supplementation with amino acids like arginine, are essential for addressing these challenges. Studies have demonstrated the beneficial effects of amino acids in wound healing, highlighting their role in promoting collagen synthesis, enhancing immune function and reducing inflammation (Table 1). Arginine, in particular, has been shown to accelerate tissue repair and improve outcomes in patients with

Table 1: Overview of studies utilizing Arginine-enriched ONS for wound treatment across various patient populations

Author's	No. of patients	Wound type	ONS	Pathology
Erdem <i>et al.</i> [9]	40	Major Burn	Arginine, glutamine and β -Hydroxy- β -Methylbutyrate (HMB) supplementation	Reduced healing time and improved collagen synthesis
Mehl <i>et al.</i> [8]	30	Hard-to-heal wounds	ONS with arginine, proline, vitamins (A, C, E), zinc, selenium	Significant improvement in wound closure and heing
Miu <i>et al.</i> [15]	87	High-grade pressure ulcers	Oral mixture of arginine, glutamine and HMB supplementation	Enhanced wound closure and reduced inflammation
Sikaroudi <i>et al.</i> [18]	76	Chronic anal fissures	Oral L-arginine supplementation	Significant tissue regeneration and pain reduction
Smith <i>et al.</i> [19]	20	Experimental skin wounds	Multinutrient beverage with L-arginine, glutamine, omega-3 fatty acids, vitamins (C, D), zinc	Faster skin barrier restoration under acute stress

compromised healing processes [7-9], making it a critical component of nutritional interventions for HNC patients. Arginine, glutamine, zinc and omega-3 fatty acids each play distinct yet complementary roles in wound healing. Arginine enhances collagen synthesis and nitric oxide production, supporting tissue repair and immune function. Glutamine serves as fuel for immune and gut cells, maintaining gut integrity and reducing infection risk. Zinc is essential for cell proliferation and immune response, with deficiency linked to delayed healing. Omega-3 fatty acids modulate inflammation, promoting resolution and tissue regeneration, especially in chronic wounds. While arginine directly supports tissue growth, the others primarily influence inflammation, immunity and systemic support, making them valuable adjuncts in comprehensive nutritional strategies for wound healing. Research evidences highlights that Arginine is not just a building block for proteins but might play a dual role by not only enhancing the immune response by stimulating T-cell function but also boosts collagen synthesis and angiogenesis, both critical for wound healing. Other nutrients (like general proteins or vitamins) may support these indirectly, but arginine acts more directly and potently in these pathways [6,7]. Thus, the research hypothesis of the study being Arginine supplementation will enhance wound healing in glottic cancer patients with post-surgical complications.

We present the case of a 76-year-old male patient diagnosed with glottic cancer (T3N0M0) with a positive response to Arginine supplementation on wound healing after persistent complications, including wound dehiscence and saliva leak, following extensive surgical treatment and radiation therapy.

Case presentation

This 76-year-old male patient, diagnosed with glottic cancer (T3N0M0), was referred for the management of wound healing complications following extensive surgical treatment and radiation therapy. He presents with significant wound healing challenges, particularly involving the left pectoralis major flap, which has been affected by wound dehiscence and a saliva leak. The wound site continues to exhibit delayed healing despite multiple interventions.

The patient was diagnosed with glottic cancer and underwent a total laryngectomy with primary TEP insertion

in May 2024. Subsequently, he received radiation therapy. On July 28, 2024, he developed a pharyngocutaneous fistula (FCF), which necessitated a left pectoralis major flap and skin graft. Despite initial post-surgical care, the patient experienced complications, including wound dehiscence and a saliva leak, requiring multiple wound explorations. These complications have persisted, with further wound exploration and bleeding control performed on August 2, 2024 and August 18, 2024.

The patient’s condition has been aggravated by ongoing complications at the surgical site, including discomfort and delayed healing. While wound care strategies, such as regular dressing changes, have provided some relief, full recovery remains slow, with no significant improvements noted. The patient has a history of diabetes (HbA1c 6.1%, controlled). Otherwise, he reports no significant comorbid conditions.

Additionally, no significant family history of cancer or chronic health conditions was reported. Upon examination, the patient is alert and oriented, with visible surgical scars from the total laryngectomy and pectoralis major flap. There is evidence of delayed wound healing, accompanied by signs of infection at the wound site.

Vital signs are stable and there is no indication of systemic infection. Palpation of the flap area reveals tenderness and the wound site exhibits moderate inflammation. The patient’s oral intake is severely restricted due to dysphagia and mucositis and his nutritional status appears compromised as a result of ongoing feeding difficulties, despite being within the normal BMI range.

The patient was diagnosed with a complex wound-healing case following a laryngectomy and flap surgery, further complicated by an FCF and delayed recovery. Additional concerns include nutritional deficiencies that are contributing to impaired wound healing.

Management and Outcome

The primary focus of the patient’s treatment was to support wound healing, given the complications associated with wound dehiscence and a pharyngocutaneous fistula. Due to the patient’s impaired ability to consume adequate oral nutrition, a percutaneous endoscopic gastrostomy (PEG) tube was placed to ensure proper nutritional support. The nutritional regimen was designed to provide optimal nutritional requirements as well as promote wound healing

and recovery. Following European Society for Clinical Nutrition and Metabolism (ESPEN) Guidelines, the patient was given a high-calorie, high-protein diet, with a total intake of 1575 kcal/day (30 kcal/ABW) and 89.2 gm of protein daily (1.7g/kg). Specifically, Glucerna was administered via the PEG tube at a rate of 65 ml per hour, providing 1560 kcal and 62.4 g of protein [10].

Additionally, to directly support tissue repair and collagen synthesis, the patient was also given Argiment AT protein powder (Figure 1 and 2: ArgiMent® AT Advanced therapy for the nutritional support of chronic wounds; Medtrition, n.d.), with one sachet mixed with 120 ml of water twice daily, providing an additional 20 g of protein. To ensure the PEG tube remained patent, 30 ml of flushing water was administered before and after each dose of Argiment AT and the tube was flushed with 50-100 ml of water every four hours. It was also necessary to hold the feeding for two hours before and after the administration of levothyroxine to prevent interference with the nutritional feed [11].

The patient's progress was meticulously monitored throughout treatment. Key indicators of wound healing, including the size and depth of the wound were regularly assessed. Initial assessments indicated significant wound dehiscence. Nutritional status was evaluated through regular measurements of albumin, prealbumin and other markers of protein synthesis, which were closely monitored for signs of improvement. Weight changes were also tracked to assess overall nutritional intake, as adequate nutrition is critical for optimal wound healing. The patient maintained a daily record of his nutritional intake and follow-up appointments were scheduled every 3-5 days to monitor his adherence to the prescribed feeding regimen, along with any changes in wound healing and general condition.

In addition, during the treatment of glottic cancer using arginine, strict infection control protocols were implemented to ensure patient safety. Sterile environments were maintained during administration, with all instruments and surfaces disinfected regularly. Healthcare providers adhered

FOR THE DIETARY MANAGEMENT OF WOUND HEALING

ArgiMent® AT is specifically formulated to provide nutrients for the dietary management of pressure injury and wounds^{1,2,3,4,5,6} that require enhanced levels of proteins, vitamins and minerals.

- Pressure injury
- Diabetic foot ulcers
- Venous ulcers
- Burns and Injuries
- Non-healing surgical wounds
- Increased protein needs
- Pre- and Post-surgical recovery

The National Pressure Injury Advisory Panel (NPIAP) recommends 1.25 to 1.5 g of protein per kg of bodyweight for wound healing. Larger draining wounds may require higher levels, up to 2.0 g of protein per kg of bodyweight to offset protein losses from wound exudates. ArgiMent AT yields a high-protein-nitrogen intervention to meet the increased nitrogen needs associated with chronic, non-healing wounds.

Dosing and Administration
Oral: Mix one packet with 180-240 mL water or juice.
Tube Feeding: Mix 1 packet with 120 mL of water. Mix well. Administer slowly via syringe. Flush with 30 mL water before and after administration. Do not mix with tube feeding formula.
Note: Products containing glutamine are to be consumed or administered immediately upon mixing to ensure maximum potency.
 One packet of ArgiMent AT contains 5.17 g of nitrogen or the nitrogen equivalent of 31.7 g of intact protein.

Ingredients: Whey Protein Concentrate, L-Arginine, L-Glutamine, Orange Juice Powder, Fructose, Citric Acid, Bimuno® (galactooligosaccharide, lactose, glucose, galactose), Orange Flavor, Calcium Ascorbate, Sucralose, Zinc Sulfate, Copper Gluconate, Yellow 6. **Contains Milk.**

Nutrition Facts
 1 serving per container
Serving Size: 1Packet (42.75 g)

Amount Per Serving

Calories 120

% Daily Values*

Total Fat 0g 0%
 Saturated Fat 0g 0%
 Trans Fat 0g

Cholesterol 25mg 8%
Sodium 40mg 2%
Potassium 87mg 2%
Phosphorus 35mg 2%
Total Carbohydrate 6g 2%
 Dietary Fiber <1g 3%
 Total Sugars 6g
 Includes 5g Added Sugars 10%

Protein 10g

Vit. D 0mcg 0% • Calcium 83mg 6%
 Iron 0mg 0% • Vit. C 250mg 280%
 Zinc 12.5mg 110% • Copper 1mg 110%
 L-Arginine 7g † • L-Glutamine 7g †

* The % Daily Value (DV) tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition advice.
 † Daily Value not established.

Pressure Injury and Wound Healing
 ArgiMent® AT

Figure 1: ArgiMent® AT a specifically formulated supplement to provide nutrients for the dietary management of pressure injury and wounds

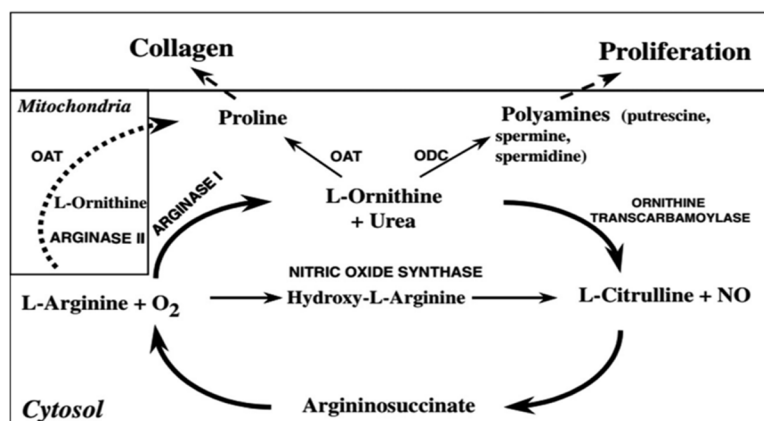


Figure 2: Advances and impact of arginine-based materials in wound healing (Zhou *et al.* [17])

to hand hygiene, used personal protective equipment (PPE), and followed aseptic techniques. Environmental factors such as temperature, humidity, and ventilation were controlled to prevent microbial growth and ensure patient comfort. Patients were monitored for signs of infection, and isolation precautions were applied when necessary. These measures helped minimize the risk of hospital-acquired infections and supported the safe and effective use of arginine in treatment protocols.

By the third week of treatment, the patient's wound showed significant improvement in terms of both size and depth. This was attributed to the enhanced nutritional support, with a particular focus on the supplementation of arginine, which directly impacted collagen formation and cellular repair. Albumin and prealbumin levels gradually improved, indicating better protein status and overall nutritional support [12]. After four weeks of continuous administration of Glucerna and Argiment AT protein powder, the wound dehiscence was substantially reduced and the saliva leak was under better control. The patient also experienced stabilization in his weight, without significant weight loss, further indicating that the nutritional intake was supporting his healing process.

At the end of four weeks, the patient's wound healing had progressed to an acceptable level and he was deemed ready for discharge. It was decided that he would continue with his nutritional supplementation at home, with follow-up appointments scheduled as needed for ongoing monitoring of his wound healing and nutritional status. The treatment plan also included continued use of the Argiment AT protein powder to maintain the wound healing benefits observed during the hospital stay.

DISCUSSION

Glottic cancers present substantial challenges in treatment, particularly when surgical interventions and adjuvant therapies result in complications such as delayed wound healing [13,14]. In this case, the patient experienced persistent wound dehiscence and saliva leakage.

Nutritional interventions, particularly arginine supplementation, have shown significant promise in addressing these challenges [8,9,15]. Arginine plays a pivotal role in tissue repair through its involvement in the arginine-NO and arginine-arginase pathways, which enhance collagen synthesis, modulate inflammatory responses and promote cell proliferation [16,17].

For instance, a clinical study demonstrated that ONS with arginine, combined with proline, zinc and vitamin C, significantly improved the healing of complex wounds without adverse effects, supporting its utility even in patients with comorbidities [8].

The benefits of arginine-enriched supplements have also been studied across various patient populations with hard-to-heal wounds. In burn patients, supplementation improved

protein markers, aiding recovery [9]. However, in elderly patients with advanced pressure ulcers, the improvements were modest compared to standard care [15], indicating that the efficacy of arginine may depend on wound type and patient condition. In the current case, the persistent saliva leakage and delayed healing responded favorably to targeted nutritional supplementation, addressing the unique challenges of extensive surgery and radiation exposure.

Further evidence of arginine's efficacy comes from its role in enhancing vascularity and reducing sphincter pressures through Nitric Oxide (NO)-mediated pathways. Studies in chronic anal fissures have shown significant reductions in pain, bleeding and fissure size with arginine supplementation [18]. These findings are consistent with the observed improvements in salivary leakage and mucosal healing in patients undergoing extensive oropharyngeal surgeries. Additionally, studies suggest that stress-related factors, such as sleep deprivation, exacerbate delayed wound healing. Nutritional supplement containing arginine accelerated healing even under acute stress conditions [19,20] highlighting its potential to mitigate exacerbating factors in complex cases. Subgroup analysis from a systematic review demonstrated that arginine supplementation at doses exceeding 15 g/day significantly improved wound healing outcomes, with superior effects compared to lower doses [7].

The patient's favorable response to arginine, despite age, diabetes and prior radiation, may stem from its immunomodulatory effects, improved microcirculation and metabolic support. Arginine may enhance T-cell function, nitric oxide production, tissue repair and vascular health, aiding healing and drug delivery. Its role in protein synthesis and stress reduction may boost resilience. Further research is needed to clarify mechanisms. However, despite potential benefits of arginine supplementation but one could not potentially ignore any possible side effects or risks, especially in cancer patients, such as promoting tumor growth in certain contexts or impacting metabolic balance. Also, futuristic studies could also be conducted on different arginine dosage protocols, combinations as well as treatment durations. Therefore, more studies are required in future to offer a more balanced and clinically cautious perspective.

CONCLUSION

Our case emphasizes the importance of early nutritional interventions, particularly arginine supplementation, in enhancing wound healing in cancer patients following extensive surgery and radiation. Using arginine significantly supported tissue repair, promoting collagen formation and immune function, which helped address wound dehiscence and saliva leakage complications. The patient's excellent tolerance to the supplementation also contributed to a favorable recovery, with a complete pathological response observed. However the exact mechanisms are unknown and needs further exploration. This case highlights the potential

of nutritional support as a valuable adjunct in improving wound healing and overall outcomes in cancer patients with complex postoperative challenges.

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