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The Impact of Malnutrition on the Wound Healing Process: A Summary of Current Knowledge

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Abstract

Background:

Wound healing is a complex, energy-dependent biological process requiring adequate availability of micronutrients and macronutrients to support angiogenesis, immune defense, collagen synthesis, fibroblast proliferation, and tissue remodeling. Malnutrition in the form of micronutrient deficiencies, protein–energy malnutrition or sarcopenia is highly prevalent among patients with chronic and acute wounds and has been closely related with poor clinical outcomes increased such as infection risk and delayed healing.

Aim:

The aim of this narrative review was to summarize current PubMed-indexed evidence on the impact of malnutrition on the wound healing process and to synthesize clinical data regarding nutritional interventions that may improve wound outcomes.

Materials and Methods:

A narrative literature review was conducted based exclusively on peer-reviewed studies indexed in PubMed. Experimental studies, observational studies, randomized controlled trials, and systematic reviews addressing nutrition, malnutrition, and wound healing were included. Evidence from the provided publications and their referenced bibliographies was analyzed and synthesized qualitatively.

Results:

Clinical and experimental evidence shows that malnutrition causes disruptions of all phases of wound healing by disturbing inflammatory control, decreasing collagen deposition, delaying angiogenesis and reducing fibroblast activity. Observational studies report a high prevalence of malnutrition among patients with chronic wounds, particularly pressure injuries and venous leg ulcers, and associate poor nutritional status with slower wound closure and higher complication rates. Randomized clinical trials and systematic reviews indicate that targeted oral nutritional supplementation, especially high-protein formulas enriched with zinc, arginine and antioxidants, improve healing effects in patients with pressure ulcers when they are used as an adjunct to standard wound care.

Conclusions:

Malnutrition is a major, modifiable risk factor for impaired wound healing. The available evidence supports routine nutritional screening and individualized nutritional therapy as integral components of comprehensive wound management, particularly in patients at risk of or diagnosed with malnutrition.

Keywords: malnutrition; wound healing; chronic wounds; surgical-site infection; micronutrients; clinical nutrition.

1. Introduction

Wound healing is a complex, metabolically demanding process, and optimal nutrition is a key determinant of successful progression through healing. Two major factors commonly compromise healing: the injury-induced stress response and the presence or development of protein–energy malnutrition (PEM). Because significant wounds trigger a hypermetabolic, catabolic state with increased nutrient requirements—and PEM is frequent in chronic wound populations, especially among older, disabled, or chronically ill patients—nutritional status cannot be separated from the normal healing process. [1]

Adequate nutritional status is essential for immune competence, angiogenesis, fibroblast proliferation, collagen synthesis, and extracellular matrix remodeling during wound repair [2].

Chronic wounds may fail to progress through the normal stages of healing in an orderly and timely manner and can remain arrested in a prolonged inflammatory state, which contributes to persistent tissue breakdown and delayed closure. In older and chronically ill populations—where chronic wounds are more prevalent—malnutrition is also more common, and the coexistence of chronic wounds and malnutrition suggests a clinically relevant relationship affecting outcomes. Therefore, comprehensive wound management should include routine nutritional assessment, and the authors emphasize that diagnosis is strengthened by combining basic clinical/anthropometric evaluation with biochemical measures and bioelectrical impedance analysis rather than relying on body weight alone. [6].

In the setting of a significant wound, the injury-induced stress response drives a hypermetabolic, catabolic state with increased energy and protein needs, so unrecognized or uncorrected malnutrition can directly limit the biological capacity to progress from inflammation to effective tissue repair. In chronic wounds, systemic factors—including poor nutritional status—interact with local wound-bed pathology and are linked to impaired host defense, reduced collagen formation, and disrupted angiogenic and reparative processes that contribute to delayed closure and chronicity. Consequently, alongside local wound management, care pathways should explicitly incorporate structured nutritional evaluation and timely nutritional support to address these systemic barriers to healing. [1,3]

Observational studies indicate that malnourished patients with wounds experience slower wound closure, higher rates of infection, increased wound recurrence, and greater healthcare utilization compared with well-nourished individuals [3,10,12].

Despite the growing body of evidence linking nutritional status with wound outcomes, malnutrition remains underrecognized and undertreated in routine wound care practice [2,7].

Current wound management strategies often focus primarily on local wound treatment, while systemic nutritional assessment and intervention are inconsistently integrated into standard care pathways [3,8].

2. Research materials and methods

2.1. Participants

This narrative review included evidence derived from adult human populations with acute and chronic wounds, such as pressure injuries, venous leg ulcers, diabetic foot ulcers, and postoperative wounds, as reported in PubMed-indexed observational studies, randomized controlled trials, and systematic reviews

Several experimental studies using mammalian wound models were also included to provide mechanistic insight into the biological effects of malnutrition on tissue repair processes.

The populations represented in the reviewed clinical studies predominantly consisted of older adults, individuals with chronic diseases, and patients in rehabilitation or long-term care settings, all of whom are at increased risk of malnutrition and impaired wound healing.

2.2. Procedure / Test protocol / Measure / Instruments

Across the reviewed literature, nutritional status was assessed using a combination of clinical history, anthropometric measurements, biochemical parameters, and body composition analysis.

Anthropometric assessments included body mass index, unintentional weight loss, and nutritional screening tools applied in clinical wound populations.

Biochemical markers such as serum albumin and prealbumin were frequently reported, although authors consistently emphasized their limited specificity due to the influence of inflammation and hydration status.

Body composition assessment using bioelectrical impedance analysis was employed in selected studies to evaluate fat-free mass and hydration status in patients with chronic wounds.

Wound healing outcomes were measured using standardized clinical endpoints, including wound area reduction, time to complete epithelialization, and validated wound assessment scales.

Experimental studies additionally evaluated histological parameters, collagen deposition, angiogenesis markers, and inflammatory mediators to characterize healing at the tissue level.

2.3. Data collection and analysis / Statistical analysis

Data from the included studies were extracted qualitatively and synthesized thematically to identify consistent patterns linking nutritional status with wound healing outcomes.

The review focused on biological plausibility, consistency of findings across study designs, and clinical relevance rather than on pooled quantitative estimates.

2.3.1. Statistical Software

The reviewed clinical studies reported the use of standard biomedical statistical software packages, most commonly SPSS, to analyze wound healing outcomes and nutritional variables.

In several studies, the specific statistical software was not explicitly stated, which is common in clinical nutrition and wound care literature.

2.3.2. AI

In this article, AI was used for two specific purposes. First, it supported the refinement of the academic English language in the manuscript to improve its clarity, adherence and consistency with scientific writing conventions, including style, grammar and presentation of results.

Second, it aided in the text analysis of the clinical reasoning narrative to identify linguistic patterns associated with specific logical errors. All AI tools were used solely as a supportive tools under constant human supervision. Final decisions regarding the study's conclusions, interpretation of results and error classification were made by experts in clinical medicine and formal logic. In this way, AI enhanced the efficiency of pattern detection, language editing, and data processing without replacing human judgment at any stage of the analysis.

2.3.3. Statistical Methods

Descriptive statistics were used to characterize patient populations, nutritional status, and wound characteristics across studies .

Comparative analyses between malnourished and well-nourished groups were performed using parametric or non-parametric tests depending on data distribution.

observations applied multivariable regression models to adjust for confounding factors such as age, comorbidities, wound severity, and treatment modality.

Randomized controlled trials evaluated intervention effects using between-group comparisons and longitudinal analyses of wound healing trajectories over time.

3. Research results

3.1. Nutritional status patterns observed in patients with chronic wounds

In a prospective cohort of 60 patients with chronic wounds (venous ulcers, diabetic foot syndrome, and pressure injury), individuals with pressure ulcers demonstrated significantly lower fat-free mass–related indices and generally poorer body composition compared with the venous ulcer and diabetic foot groups. [6] In the same study, the pressure ulcer subgroup also showed the lowest reported values of key biochemical and nutritional indicators, including albumin (3.20 g/dL), hemoglobin (10.81 g/dL), and the Nutritional Risk Index (NRI) score (88.13 points), consistent with a higher risk of malnutrition in this clinical phenotype. [6]

Across the reviewed evidence, wound healing was repeatedly framed as nutritionally contingent: major wounds were associated with a hypermetabolic, catabolic state and increased nutrient requirements, while concurrent protein–energy malnutrition (PEM) was linked to loss of lean body mass and reduced capacity to support repair processes. [1]

3.2. Clinical effectiveness of nutrition-focused interventions in pressure ulcers and mixed wound populations

Evidence from randomized controlled trials summarized in a systematic review and meta-analysis indicates that disease-specific nutritional support (high-calorie/high-protein formulas enriched with arginine, zinc, and antioxidants) was associated with improved pressure ulcer (PU) healing outcomes versus control nutritional interventions. [11] Specifically, pooled results from three eligible trials showed a significantly greater reduction in PU area at 8 weeks (mean difference −15.7% [95% CI, −29.9 to −1.5]; P=0.030; I^2=58.6%) and a higher likelihood of achieving ≥40% reduction in PU size at 8 weeks (OR=1.72 [95% CI, 1.04 to 2.84]; P=0.033; I^2=0.0%). [11] A nearly significant difference was observed for complete healing at 8 weeks (OR=1.72 [95% CI, 0.86 to 3.45]; P=0.127), while change in area at 4 weeks did not reach statistical significance (−7.1% [95% CI, −17.4 to 3.3]; P=0.180). [11]

In a rehabilitation hospital retrospective analysis including 341 inpatients with chronic wounds (treatment group: 114 patients with 322 wounds; control group: 227 patients with 420 wounds), daily use of a wound-specific oral nutritional supplement (WS-ONS) for ≥14 days was associated with better wound size improvement during hospitalization. [10] At discharge, percent wound area reduction was nearly two-fold greater in the WS-ONS group compared with usual diet alone (61.1% vs 34.5%), and weekly wound improvement (reduction in wound area or wound volume) was more likely in the WS-ONS group, particularly early in care (start to week 2). [10]

A case report describing "rehabilitation nutrition" in a malnourished patient with type 2 diabetes and a severe pressure ulcer reported clinical improvement in physical function and wound healing under a structured energy/protein prescription combined with daily rehabilitation. [14] The authors reported that the pressure ulcer epithelialized by day 14 after discharge, while also noting the need for close metabolic (glycemic) management during escalation of caloric/protein targets. [14]

3.3. Nutrition support as part of complex management in venous leg ulcers

In a 12-week prospective study of 35 individuals with venous leg ulcers (VLU), a complex intervention combining professional wound care and a specialized oral nutritional supplementation regimen (three times daily 200 mL of an energy-dense, protein-rich formula containing arginine, zinc, and vitamins) was associated with measurable improvement in wound healing dynamics. [12] Complete wound healing occurred in 6 patients, and median ulcer area decreased from 26.5 cm^2 to 14.8 cm^2 (p=0.0001); the highest healing rates and the most marked increase in prealbumin were observed in the first 6–8 weeks. [12] Wound healing progress coincided with decreased pain intensity and improved quality of life, and supplementation was reported as well accepted. [12]

A systematic review focused on nutritional condition and compression treatment in venous ulcer recovery identified 12 included studies after full-text assessment and highlighted heterogeneity in both nutritional exposures and compression modalities. [13] The review emphasized that outcomes differed depending on compression type and pressure intensity, and it concluded that more clinical studies are needed to clarify comparative effects and to evaluate a broader range of dietary factors under more comparable conditions. [13]

3.4. Experimental evidence on malnutrition-associated impairment and (in)adequacy of short-term refeeding

In an experimental model of acute open wounds in rats, prior malnutrition was associated with a prolonged inflammatory response, impaired fibroblast increase between post-trauma days 7 and 14, decreased collagen III expression, and reduced wound contraction compared with eutrophic controls. [5] Importantly, short-term enteral refeeding—even with a specialized enteral diet enriched with arginine and antioxidants—failed to improve wound healing in malnourished rats, supporting the interpretation that short duration nutritional repletion may be insufficient to reverse malnutrition-related impairments in early healing phases. [5]

Complementary review-based evidence also underscores the high energy demands of wound repair and the risk that depleted reserves in malnourished patients may be inadequate to meet requirements without a targeted nutritional plan (e.g., energy expenditure cited up to 35–40 kcal/kg/day in the wound-healing context). [15]

4. Discussion

Malnutrition should be interpreted as a systemic, potentially modifiable determinant of wound outcomes rather than a “background” comorbidity. Evidence from mechanistic syntheses emphasizes that clinically meaningful tissue loss and metabolic stress can shift wound healing toward delayed, inefficient repair—especially when the wound coexists with inflammation, infection risk, or chronic disease burden. In this framework, the wound competes for substrates with other essential physiological demands, and inadequate energy–protein availability amplifies catabolism and undermines anabolism, thereby increasing the likelihood that wounds fail to progress through timely closure and durable remodeling [1].

A key implication is that nutritional intervention cannot be conceptualized as a short, isolated add-on to local wound care. Experimental work illustrates that prior malnutrition can “imprint” impaired healing biology: in a rat model, refeeding—even with a specialized enteral diet—did not normalize healing in previously malnourished animals and was associated with persistence of a prolonged inflammatory phase and impaired repair, suggesting that restoring intake alone may be insufficient once systemic deficits and inflammatory dysregulation are established [5]. When translated to clinical care, these findings support a more proactive approach: screening and early correction of deficits, coupled with sustained nutritional support, rather than late and brief supplementation introduced after chronicity develops.

The clinical studies included in this review collectively indicate that malnutrition in chronic wound populations is heterogeneous and not reliably captured by body weight alone. In a comparative study of pressure injuries, diabetic foot ulcers, and venous leg ulcers, bioelectrical impedance analysis (BIA) and standardized nutritional tools demonstrated distinct body-composition and nutritional-risk profiles across etiologies. Importantly, phase angle correlated strongly with nutritional indices and albumin across the overall sample, supporting the concept that functional body-composition markers may align with clinically meaningful nutritional vulnerability in wound patients [6]. The observation that venous leg ulcer patients can present with relatively high adiposity alongside impaired lean-mass indices underscores why reliance on BMI alone can misclassify risk and why multimodal assessment (clinical screening + biochemical data + body composition) is clinically rational [6].

Regarding interventional evidence, the most consistent randomized evidence supports disease-specific, high-calorie/high-protein formulas enriched with arginine, zinc, and antioxidants for pressure ulcer healing. A systematic review and meta-analysis of randomized controlled trials found that such formulas were associated with a significantly greater reduction in pressure ulcer area and a higher probability of achieving ≥40% reduction in ulcer size at 8 weeks versus control nutrition interventions that met energy requirements [11]. Although complete healing at 8 weeks did not reach conventional statistical significance in that analysis, the direction of effect and the improvement in intermediate healing endpoints support clinical utility, particularly when integrated into comprehensive pressure injury management [11]. These findings align conceptually with broader mechanistic arguments that "wound-targeted" substrates (adequate protein/energy plus selected conditionally essential amino acids and micronutrients) may influence granulation and matrix deposition during the proliferative phase [1].

Real-world data from a rehabilitation setting further suggest that oral nutritional supplementation formulated for skin integrity can be associated with faster week-to-week improvement in wound size. In a propensity-weighted regression analysis, patients receiving a wound-specific oral nutritional supplement (WS-ONS) showed higher odds of wound healing in early weeks (e.g., week 1–2) compared with controls, with the relative advantage diminishing over subsequent weeks [10]. This pattern may reflect the clinical reality that patients in rehabilitation often present with high baseline complexity (multiple wounds, larger wounds, higher illness severity), and early nutritional support may be most impactful when catabolic pressure is greatest. However, the observational design, potential residual confounding (including differences in disability and wound burden), and variability in exposure duration mean causality cannot be asserted; instead, the findings strengthen the argument that nutrition should be embedded early in multidisciplinary pathways rather than delayed [10].

For venous leg ulcers (VLUs), the evidence base is expanding but remains methodologically diverse. In a 12-week prospective study integrating oral nutritional supplementation (including an arginine- and micronutrient-containing formula) into complex therapy, the median ulcer area decreased substantially over time, and improvements were observed in patient-reported outcomes (including quality-of-life domains) alongside biochemical nutritional markers during treatment, consistent with clinically meaningful benefit when nutrition is combined with standard VLU care [12]. A systematic review examining nutritional condition alongside compression therapy similarly concluded that nutritional status is meaningfully associated with VLU recovery, while also highlighting heterogeneity across compression modalities, intensity, and patient metabolic features (including hyperhomocysteinemia) [13]. Notably, the review reports that correction of vitamin B12 and folate deficiencies in the setting of hyperhomocysteinemia was associated with improved healing outcomes in included studies, suggesting that targeted micronutrient correction may be relevant in selected VLU subgroups [13]. Together, these data support a pragmatic interpretation: nutritional assessment and correction are likely beneficial adjuncts in VLU care, but high-quality trials that standardize nutrition exposure, compression protocols, and wound endpoints are still needed to clarify effect sizes and identify responders.

The included case report adds a clinically useful perspective on implementation challenges in complex metabolic disease. In a malnourished patient with type 2 diabetes and a severe pressure ulcer, a structured “rehabilitation nutrition” program (energy/protein prescription aligned with activity and rehabilitation goals) accompanied by close glycemic management was associated with functional recovery and pressure-ulcer epithelialization after discharge [14]. While case reports cannot establish generalizable efficacy, they highlight an important clinical point: nutrition support must be individualized and coordinated with disease control (e.g., diabetes therapy), because aggressive repletion can conflict with glycemic targets, and underfeeding can compromise both physical function and tissue repair [14].

Across wound etiologies, a consistent systems-level message emerges: nutritional screening and assessment should be routine, not optional, and should trigger timely referral and intervention. Practice-oriented synthesis emphasizes that validated screening tools (e.g., MUST) and multidisciplinary coordination—often led by dietitians—are central to preventing missed malnutrition and ensuring that macro- and micronutrient strategies are aligned with wound stage, comorbidity burden, and care setting [15]. Importantly, this does not imply that nutrition replaces local treatment; rather, the literature supports an integrated model in which debridement, offloading/compression, infection control, and metabolic optimization are complemented by structured nutritional assessment and sustained nutritional support [1,12,13,15].

Future research should prioritize (1) standardized definitions of malnutrition and sarcopenia in wound cohorts, (2) harmonized wound endpoints and follow-up windows that match biological healing time frames, (3) stratified trials that test nutrition formulas and micronutrient correction within clearly defined wound etiologies, and (4) pragmatic studies that measure adherence, feasibility, and cost implications in real-world pathways. Given the signals observed for pressure ulcers in randomized evidence [11] and for VLUs in prospective clinical practice settings [12], the most clinically actionable direction is not to debate whether nutrition matters, but to determine which patients benefit most, which nutrition targets are most predictive of response (including functional body-composition markers such as phase angle), and how to implement nutritional care reliably across settings without delaying definitive local wound therapy [6,10,11,12,13,15].

5. Conclusion

Malnutrition is a clinically relevant and potentially modifiable systemic factor that can compromise wound healing by sustaining catabolism and limiting the substrates required for effective tissue repair. [1,15]

Evidence from experimental models indicates that pre-existing malnutrition can induce persistent impairments in healing biology and that short-term refeeding may be insufficient to reverse these effects, supporting the need for early identification and sustained nutritional

correction. [5]
Clinical data show that patients with chronic wounds—particularly those with pressure injuries—frequently demonstrate unfavorable nutritional and body-composition profiles, and that more advanced assessment (including bioelectrical impedance analysis) can add clinically meaningful information beyond weight-based metrics. [6]
Interventional evidence is strongest for pressure injuries, where disease-specific, high-protein oral nutritional formulas enriched with arginine, zinc, and antioxidants improve key healing outcomes when used as an adjunct to standard wound care. [11]
In rehabilitation and real-world inpatient settings, the use of wound-specific oral nutritional supplementation has been associated with greater early wound-size improvement compared with usual diet alone, although confounding cannot be fully excluded in observational designs. [10]
For venous leg ulcers, nutritional support combined with standard compression-based management may contribute to improved healing dynamics, but heterogeneous methodologies and exposure definitions highlight the need for more standardized and adequately powered clinical trials. [12,13]
Overall, comprehensive wound care pathways should incorporate routine nutritional screening, structured assessment, and individualized nutritional therapy alongside local wound management and treatment of underlying disease to optimize healing outcomes and reduce chronicity. [1,6,15]

Supplementary Materials

Not applicable

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