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Review Article

# Old Age, Malnutrition, and Pressure Sores: An Ill-Fated Alliance

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**Wound healing is a complex, tightly regulated process, consisting of three distinct phases. In each phase of wound healing, energy and macronutrients are required. Moreover, animal studies have established a specific role for certain nutrients such as the amino acid arginine, the vitamins A, B, and C, and the elements selenium, manganese, zinc, and copper. Chronic wounds such as pressure ulcers have extensively been investigated as to the risk of development, prevention, and cure. Here, the combination of old age, malnutrition, and pressure ulcers is highly unfortunate. Energy and nutrients, such as proteins and vitamins B and C, being deficient at old age are needed in pressure ulcer healing. Malnutrition is associated with skin anergy and with immobility because of mental apathy and muscle wasting. Severe malnutrition, impaired oral intake, and the risk of pressure ulcer formation appear to be interrelated. Adequate nutrition may reverse the underfed state unless an underlying wasting disease was present and appeared to reduce the prevalence and incidence in cross-sectional and prospective observational studies. However, attempts to prevent pressure ulcers by nutritional intervention were divergent in outcome, reflecting the difficulties to meet the daily requirements in elderly persons and the lack of knowledge about true nutritional needs in wound healing. The consumption of a diet high in protein and energy may promote pressure ulcer healing. When considering nutritional support, oral supplementation should be weighted against tube feeding, as the associated morbidity of tube feeding, i.e., diarrhea, fecal incontinence, and restricted mobility being in themselves risk factors for pressure ulcers, might obscure the favorable effects of adequate nutrition. Despite the evidence in animal studies, none of the above-mentioned specific nutrients promoted the healing of pressure ulcers in humans. Therefore, the attention should be focused on early recognition of a depleted nutritional status and an adequate and supervised intake of energy (35 kcal/kg) and protein (1.5 g/kg) with provision of the recommended daily allowances of micronutrients and with correction of the nutrient deficiencies of old age.**

ALTHOUGH the consistent relationship between poor nutritional status and risk of complications forms the cornerstone of nutritional support, there is controversy about the role of nutrition in wound healing. The purpose of this article is to review the nutritional aspects of pressure ulcer healing, to discuss the assessment of the nutritional status in elderly people at risk of malnutrition and pressure ulcer development, and to evaluate the merits of nutritional support to avert malnutrition and pressure ulcer formation and to promote wound healing.

## Wound Healing

The healing of a wound is a complex, tightly regulated process, integrating cellular and systemic responses to injury (1–4). Three distinct phases can be discerned, and macronutrients are required in every phase. Proteins, amino acids, and nucleic acids are essential for protein synthesis, and fats are needed for cell membranes. Carbohydrates and fats provide the necessary cellular energy (4). Animal studies have demonstrated that micronutrients are specifically related to each phase (1,2,5–8).

The earliest response to skin injury is inflammation with wound exudation and fibrin clot formation requiring an adequate circulation. Specifically related to this phase are vitamins C and E, selenium, arginine, cysteine, and methionine. The proliferative phase is characterized by angiogenesis, fibroblast proliferation, collagen synthesis, wound matrix formation, and epithelialization, and requires vitamins A and C, thiamine, pantothenic acid, zinc, manganese, and arginine. The extensive reconstruction of the proliferative phase appears to be particularly sensitive to nutritional deficiencies. The final phase of maturation and remodeling involves cross-linkage of collagen fibers, wound contraction, and development of tensile strength. Vitamins A and C, zinc, copper, and manganese are needed. Studies on wound healing have mainly focused on vitamins A and C, zinc, and arginine (7,9–12).

Most of our knowledge with regard to the relationship between nutrition and wound healing comes from animal models (8,13,14). Here, the link between nutrition and outcome is evident: low protein diets, energy restriction, and chronic protein malnutrition interfere substantially with wound healing. In humans, the situation is quite distinct from animals: the effect of short-term starvation is less severe and collagen formation takes twice as long (8,14). Therefore, the results of micronutrient supplementation in animals might not be extrapolated straightforward to the human situation.

## Chronic Wound Healing

Pressure sores are examples of chronic wounds and have been extensively investigated as to risks of development, prevention, and treatment (15). Mainly, external factors such as pressure, shear, and friction forces govern the risk of pressure sores (1). Internal factors such as old age, immobility, incontinence, catabolic illnesses, malnutrition, and assistance with eating determine patient's susceptibility to develop pressure ulcers and are difficult to influence, nutrition being an exception. Within the prospects of an aging community, the ill-fated combination of a high prevalence of pressure sores in hospitals (3%–14%) and nursing homes (20%–33%) with a high prevalence of malnutrition (30%–50% and 19%–59%, respectively) should be a matter of concern to physicians, health authorities, and politicians (16–21).

## Assessment of Nutritional Status

The dismal combination of old age, malnutrition, and pressure ulcers calls for a separate consideration of age and nutritional status. Elderly people are at nutritional risk when they have a body mass index (BMI) below 24 $kg/m^2$ (22). Optimal ranges are between 24 and 29 $kg/m^2$. Also, elders tolerate less well small body weight losses of 5% (21,23). When the daily energy intake falls below a critical level of approximately 1500 kcal, present in 28% of women and 10% of men in the SENECA [Survey in Europe on Nutrition and the Elderly, a Concerted Action] study, it is hard to meet the recommended daily allowance (RDA) (24–26). Therefore, it is not surprising that micronutrient deficiencies have been reported from medical departments for elderly people and nursing homes (vitamin $B_6$ [32%–68%], $B_{12}$ [25%], C [32%], D [72%], and folic acid [5%–28%]), not only because of altered needs and decreased intestinal absorption but also as a result of an altered appetite regulation and anorexia of aging; it also partly reflects the adverse effects of being dependent on eating assistance (26–31).

The assessment of nutritional status is composed of: 1) screening for nutritional problems by taking the health history; 2) assessment of somatic protein and fat compartments through anthropometry; and 3) biochemical measurements of visceral proteins and immune competence (23,32,33).

By taking the *health history*, one should be informed about usual weight and recent weight changes, increased metabolic needs, and increased losses (23,32,34). Also, information about concomitant diseases, past major surgery, social, and dietary history should be obtained. Causes for concern are:

- Weight loss of $\geq$ 5% in 1 month; $\geq$ 7.5% in 3 months, and $\geq$ 10% in 6 months;
- BMI of $\leq$ 21 $kg/m^2$ or a body weight $\leq$ 80% of usual weight;
- Intake consistently less than 60% of the RDA;
- Reduction in food intake to 50% of normal in the last week; or
- Starvation for 3 days in malnourished and 5–7 days in well-nourished participants (23,32–35).

To assess the *somatic protein and fat compartment*, the arm muscle and fat area can be calculated from the mid-arm circumference and triceps skinfold.

Biochemical measurement of *visceral proteins and cell-mediated immunity* ideally requires a marker, highly specific for nutritional changes, with a short half-life and a small pool. Serum prealbumin and retinol-binding protein as well as a battery of skin test antigens are used. Low levels of lymphocytes, cholesterol, hemoglobin, and albumin are often quoted as independent predictors of pressure ulcer risk (18,19,36–38). A low serum albumin has long been suggested to promote pressure ulcer formation through interstitial edema, reduced tissue oxygenation, and nutrient flow, confirmed in cross-sectional studies (18,37). Others showed a lower albumin to be related to higher stages of pressure ulcers in cross-sectional studies (39), which could not be confirmed in longitudinal and prospective studies (40,41). Nowadays, a low serum albumin is considered to be the result of severe illness, protein exudation in wounds, and previous low intake of proteins.

Rather than assessing the actual nutritional status, individuals at risk of malnutrition should be recognized. Prognostic nutritional indexes include a questionnaire and physical examination (Subjective Global Assessment) (42,43), weight combined with laboratory (Nutritional Index) (44), or laboratory with anthropometry (Likelihood of Malnutrition) (45). The Mini Nutritional Assessment with questions on anthropometry, diet, and well-being is exclusively developed for elderly people (46). The original pressure ulcer risk scale of Norton did not take food intake into consideration (47). The modified Norton scale and the Waterlow and Braden scales consider nutrition as well (48–50).

## Relationship Between Nutritional Status and Pressure Sores

The observed prevalence of pressure ulcers raises the question whether nutritional status correlates with development of pressure ulcers, and if so, whether nutrition plays a role in prevention and healing.

### *Malnutrition as a Risk Factor for Pressure Ulcers (Table 1)*

Many studies on malnutrition as a risk factor for pressure sores are available. Two longitudinal studies in the community and nursing homes did not find malnutrition to be associated with the formation of pressure ulcers (38,51). Longitudinal studies, using the Minimal Data Set in nursing homes, showed a better nutritional status reflected by a higher BMI to constitute a lower risk (52,53). Five cross-sectional and one prospective study investigated the impact of malnutrition, assessed by anthropometry and biochemistry (18,36,37,39,54,55). A sixth cross-sectional study defined less optimal nutrition by having poor appetite or being fed by nasogastric or intravenous routes (56). One case-controlled and two prospective studies looked at impaired nutritional intake of energy and/or proteins (57–59). Notwithstanding differences in study design and methodological flaws, all studies showed an increase in existing or newly developed ulcers in malnourished participants and in participants with lower intakes of

Table 1. Prospective Studies on Malnutrition as a Risk Factor for the Development of Pressure Ulcers

| Study Characteristics | Malnutrition Assessed by | Incidence of Ulcers | Methodological Remarks |
|---|---|---|---|
| Hospital admission, prospective, $N = 286$, age 74 ± 9 y, study 8 wk (36) | Anthropometry and biochemistry | 1.4% at day 7, 17.1% at day 14, and 43.7% at day 21 in participants ≤58 kg vs 0.5%, 8.6%, and 11.8%, respectively, in participants >58 kg (RR 2.2; 95% CI 1.1/4.0) | 619 eligible; 333 nonconsenters more likely to have been admitted from nursing homes; of 286 participants, 192 remaining at day 7, 70 at day 17, and 37 at day 21 |
| Hospital admission, prospective, $N = 61$, age 76 ± 13 y, study 76 d (58) | Anthropometry and biochemistry | 17% in malnourished vs 9% in nonmalnourished patients (RR 2.1; 95% CI 1.1/4.2) | Comorbidity and severity of illnesses and activities of daily living similar in both groups |
| Chronic care hospital, cross-sectional, $N = 301$ and prospective, $N = 199$, age 71 ± 17 y, follow-up 3 wk (37) | Poor intake over last 3 weeks due to persistent anorexia, gastrointestinal disturbances with intake of less than 1100 kcal or 50 g protein; biochemistry | 10.8% developed PU at 3 weeks | PU associated with creatinine, but not albumin; MLR: factors positively associated being an impaired intake (OR 2.8; 95% CI 1.0/17.9), immobility (OR 3.8; 95% CI 1.0/14.0), and a history of cerebrovascular accident (OR 5.0; 95% CI 1.7/14.5) |
| Nursing home admission, prospective, $N = 200$, age > 65 y, study 12 wk (59) | Dietary intake of calories, protein, copper, iron, zinc, folacin, and vitamins A, $B_1$, $B_2$, $B_6$, $B_{12}$, and C as % of recommended daily allowance; anthropometry and biochemistry | 35% developed stage I and 38.5% stage II PU | PU associated with lower intake of energy and protein, with lower serum albumin and anthropometry, stage I PU associated with intake of Vitamin C; MLR: risk predicted by Braden scale, age, blood pressure, body temperature, and dietary protein and iron intake |

*Note*: RR = relative risk; CI = confidence interval; MLR = multiple logistic regression; OR = odds ratio; PU = pressure ulcer.

proteins and energy. However, the odds ratios for other well-known risk factors such as cerebrovascular accident, immobility, and assistance with activities of daily living were much higher than the odds ratios for nutritional status. The role of malnutrition in the development of pressure ulcers is rather complex: pressure, shear, and friction forces on protuberant bones cause more ischemic destruction with more necrosis and less epithelialization (41). Anemia, hypoalbuminemia, lymphopenia, and skin anergy interfere with adequate oxygenation, blood and nutrient flow, and immune defense. Mental apathy and muscle wasting may increase through anorexia and immobility. Comorbidities causing the malnourished state contribute as well.

### *Nutrition to Prevent Pressure Ulcer Formation*

Failure to distinguish an underfed state from cachexia explains why nutritional interventions show little benefits (30,60). Poor intake may predispose to impaired wound healing, but the subsequent underfed state can be reversed by adequate intakes. Cachexia, however, is a wasting syndrome due to hormonal and metabolic abnormalities and cytokines; adequate nutrition will not correct this.

Larsson and colleagues investigated 501 patients of whom 28.5% were malnourished at admission to a long-term medical ward (61). Malnutrition was defined by anthropometry, visceral proteins, and recall antigen skin tests. Pressure sores were significantly more present in malnourished (38.4%) than in well-nourished patients (20.6%) and significantly more in anergic (28.0%) than skin-reactive (18.8%) patients. Malnourished and well-nourished participants were divided into a group receiving a 3-meal hospital diet of 2200 kcal and a group that received an extra supplement of 400 kcal and 16 g protein, twice daily, on top of the hospital diet, for 26 weeks. After 8 weeks, 82% of malnourished patients remained malnourished when eating the hospital food, whereas 41% of those taking the supplement reversed their underfed state. In the group of initially well-nourished patients, 26% developed a state of malnutrition on the hospital food, but the nutritional status could be maintained in 92% of those taking the extra supplement. Patients who received the supplement tended to develop fewer sores and to heal to a greater extent (54). Delmi and colleagues reported fewer pressure ulcers and a significantly better clinical outcome when older patients with femoral neck fractures were given an oral supplement of 254 kcal and 20 g of protein in the evening for a mean of 32 days (62). Recently, a short, 15-day nutritional intervention with 2 oral supplements of 200 kcal added to a 1800 kcal hospital diet in 672 critically ill older inpatients showed similar results: a tendency to have less pressure ulcers at day 5, 10, and 14 (63). Apart from hypoalbuminemia, a low Norton score, high activities of daily living dependency, and having a low limb fracture, belonging to the control group implied a significant risk for pressure ulcer development. The latter study also clearly showed the problems in achieving nutritional goals despite offering adequate quantities. Approximately 62% of the required 1800 kcal and 45 g of protein was attained in the nonsupplemented group, but 63% of the required 2200 kcal and 63 g of protein in the supplemented group (63). The effect of supplemented tube-feeding (1500 kcal, 60 g protein) during nighttime for 2 weeks was investigated by Hartgrink and colleagues in patients with hip fractures (64). All patients received a standard hospital diet in daytime. Despite a low acceptance of the tube (25/62 patients accepted the tube for 1 week and only 16/62 for 2 weeks) intakes of energy and protein were 2–3 times higher and nutritional status was largely improved, however, without any effect on pressure ulcers.

Therefore, in the short term, nutritional support might be of value to avert or reverse nutritional deterioration. An early reduction in pressure ulcers was, presumably, not to be

Table 2. Prospective Studies Concerning the Influence of Nutrition on the Healing of Pressure Ulcers

| Study Characteristics | Improved Healing Rate by | Methodological Remarks |
|---|---|---|
| Prospective randomized, PU treatment, $N = 72$, duration median 13 d (67) | Every 100 mmol/d higher protein N intake (8.8 g protein) increase at baseline (OR 1.4; 95% CI 1.1/1.8) | Study planned to compare conventional treatment with air-fluidized beds, feeding not a primary goal, no records given on subsequent diet; OR of improvement in total surface area by air-fluidized beds 5.6 (95% CI 1.4/21.7), OR of lower leucocyte count 1.3 (95% 1.1/1.6) |
| Prospective, $N = 52$ with 128 PU (68) | Adequate diet, fulfilling energy and protein requirements and mostly consumed by the patient; healing rate 89% in adequate vs 58% in inadequate nutritional support | Study planned to compare hydrocolloid and wet-to-dry dressings; nutritional factors being a secondary end-point; influence of anorexia, disease, or inability to feed oneself not given; no correlation with initial nutritional status |
| Tube fed, randomized controlled, $N = 12$, duration 8 wk (69) | 25 en% (1.8 g/kg) very high protein diet with a 73% decrease in ulcer size, a healing of 67%, and a positive N balance in all, compared to a 16 en% (1.2 g/kg) high protein diet with 42% decrease in ulcer size, no complete healing, and a positive N balance in 67% | High protein group having larger ulcer sizes (1.6–63.8 $cm^2$ vs 1.0–46.4 $cm^2$ in very high protein group) |
| Tube fed or meal supplements, controlled, $N = 48$, duration 8 wk (70) | 24 en% protein diet showing a 4.2 $cm^2$ greater and in stage IV a 7.6 $cm^2$ greater decrease in total truncal ulcer surface area compared to 2.1 $cm^2$ and 3.2 $cm^2$ on a 14 en% protein diet | Many flaws: 28 patients completing the study, no intention-to-treat analysis, great number of potential patient subsets, no mentioning of infection or sepsis; PU healing assessed by body surface affected with summing up multiple ulcer stages, patients on 24 en% protein also receiving more minerals and vitamins |
| Tube-feeding dependent, malnourished, longitudinal, $N = 46$, duration 12 wk (71) | No effect of 123% of RDA for energy, 170% of RDA for protein, and 104% of RDA for vitamins and minerals; 65% at least 1, and 25% 3 or more pressure ulcers at the start, after 12 wk 61% and 27%, respectively | Prospective follow-up of nutritional status and its relationship with outcome; 65% PU prevalence positively related to weight loss and negatively to blood levels of cholesterol, zinc, retinol, α tocopherol, and iron; MLR: α tocopherol associated with PU prevalence, no factor related to 12-wk ulcer prevalence or incidence |

*Note*: En% = percentage of total energy; OR = odds ratio; CI = confidence interval; MLR = multiple logistic regression analysis; PU = pressure ulcer; RDA = recommended daily allowance.

expected, as first invisible nutritional deficits had to be corrected, to be followed later, if at all, by an effect on pressure sores.

Two meta-analyses investigated nutritional interventions in elderly persons (65,66). Pressure ulcers were included in the complications. In view of the poor quality of most studies, the cautious conclusion was that oral multinutrient supplements reduced the unfavorable outcome, with oral protein-enriched feeding and tube feedings having no effect. In elderly people at risk from malnutrition, extra protein and energy in the form of sip-feeds resulted in a small weight gain, a beneficial effect on mortality and length of hospital stay without an effect on complications.

### *Nutrition to Promote Pressure Ulcer Healing (Table 2)*

Five studies investigated the rate of healing by a volitional increased intake through normal food or involuntary increased intakes through tube feeding (67–71). The intervention period varied considerably. In two studies, pressure ulcer treatment was the primary goal, nutrition being a secondary end-point (67,68). In Chernoff's study (69), randomization was inadequate as the low-protein group had larger ulcer sizes. In Breslow's study (70), the effect of intervention was not properly assessed, as multiple ulcer stages were combined to affected body surfaces. Despite being too heterogeneous to allow adequate comparisons, those studies that increased the protein intake via normal food, supplements, or sip feedings, tended to show an improved healing rate (Table 2) (67–70). Tube feeding resulted in a high rate of tube feed intolerance and in many added complications such as fecal incontinence, diarrhea, and restricted mobility (71)—factors also implicated in pressure ulcer risk—thus explaining why tube-feeding might fail to show accelerated ulcer healing.

## Nutritional Requirements

Well-designed studies establishing the nutritional needs of patients with pressure sores are lacking. Two studies investigated quadriplegic patients, prone to develop pressure ulcers. Their energy needs are usually not a problem because of a lower energy expenditure (72,73). However, when quadriplegics developed pressure ulcers, energy needs increased to levels at or above normal levels. Ignorance of these facts might be responsible for a poor nutritional status determined by depressed prealbumin, albumin, and zinc levels (74). Studies that showed a positive influence of nutritional intervention on pressure ulcers advised intakes of 30–40 kcal/kg and 1.2–2.1 g protein/kg (13,14,69,70,75,76).

Many specific nutrients have been studied in relation to wound healing in animals (6,14). The limited studies with specific nutrients in humans with arginine (12,77–79), vitamin C (80,81), and zinc (9–11) used pharmacological rather than nutritional doses. None of these specific nutrients consistently accelerated the healing of pressure ulcers, because supplementation in nondepleted patients does not make sense. Supraphysiologic doses may have opposite effects and may inhibit wound healing as is known for zinc. On the other hand, one should be aware of deficiencies that are prone to go undetected. Yet, the combination of all these specific nutrients into nutritional supplements by food industries lacks sound scientific evidence.

## Epilogue: Nutritional Recommendations

To summarize, one should be aware of the resemblance of nutrient deficiencies of old age (protein, energy, vitamins $B_6$, $B_{12}$, C, D, and folic acid) to the nutrients involved in wound healing (protein, energy, arginine, vitamins A, B, C, and zinc). Some of these deficiencies may go undetected for a considerable time. Malnutrition is strongly associated with the risk of pressure development. Screening for malnutrition should be part of the risk assessment of developing pressure ulcers. Waterlow, Braden, and modified Norton scales should be supplied with specific scales such as the Mini Nutritional Assessment. Measurements of weight, height, and weight losses over time, and blood samples for hemoglobin, albumin, lymphocytes, and cholesterol, being aware of its constraints, are mandatory. There is still a good deal of work on hand, shown by investigations on quality of care indicators: in 13%, values of lymphocytes were missing, and in 32%, values of albumin were missing, but more importantly, no information on body weight was present in 73% (82).

Being aware of the fact that nutritional needs of pressure ulcer patients have not been addressed, much would be gained, if energy (35 kcal/kg) and protein requirements (1.5 g/kg) would be met, which is difficult but feasible with a normal daily (supervised) food intake. Also, supplements can be given on top of the standard diet, preferably in the evening to not interfere with daytime intake.

An adequate intake to meet the requirements and to correct (hidden) deficiencies is of paramount importance: Studies that examined the influence of nutrition on preventing pressure ulcers might have studied severe states of malnutrition or did not succeed in providing the required amounts. In studies looking at healing of ulcers, a beneficial effect was seen in those studies that showed a supervised adequate intake. However, when the intake was less than prescribed or absorption was compromised by diarrhea due to intolerance of tube feeds, positive effects on ulcer healing disappeared.

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