5. Treatment of Malnutrition: Chronic Non-malignant Illness

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Summary

Many illnesses activate biochemical and physiological mechanisms that influence the body's ability to process energy and nutrients. As a result, the metabolism of invalids often differs from that of healthy individuals. Chronic illness may involve long periods during which metabolism shifts to a catabolic state (i.e. decay processes predominate). This leads to an increased risk of malnutrition, making the prospect of recovery less likely. Since the degree of risk is related to the severity of illness, the causal relationship between malnutrition and lowered prognosis is complex. It is therefore not entirely certain that treatment for malnutrition will increase the patient's state of health and prognosis. As with all medical questions, recommendations for nutritional treatment must rest on solid scientific grounds.

This chapter reviews the results of 65 studies of nutritional treatment administered to chronically ill older patients, most of whom were undernourished. The emphasis is on controlled random-sample studies; but studies in which the level of control was not no strict are also discussed. The studies must be evaluated in light of the considerable methodological problems associated with the execution, interpretation and comparison of such research.

Definitions of malnutrition vary, and it is a condition that is associated with illness-related catabolic processes that are difficult to control. Further, interpretation is complicated by uncertainty surrounding patients' compliance with prescribed treatment, other measures being applied at the same time which may have interactive effects, small and often heterogeneous study samples, diverse methods of treatment, short treatment times, and anthropometric and biochemical variables whose relation to prognosis is not always clear.

Despite such reservations, available studies of treatment indicate that positive results can be achieved with dietary supplements, including those in liquid form, which are administered to patients with potential or established malnutrition. Such treatment can improve breathing function in patients with chronic obstructive lung disease. It has been shown that

nutritional therapy can accelerate the recovery of older women with hip fractures, and improve the functional capacity of older persons of both genders with multiple illnesses.

However, the current state of knowledge is limited. There is a great need for prospective, controlled, randomized long-term studies of the effects of structured nutritional programmes for the treatment of older patients with both single and multiple illnesses. In addition to determining outcomes as measured by anthropometric and biochemical variables, emphasis should be placed on such clinically relevant factors as morbidity, functional capacity, health-related quality of life, time spent in care, and mortality. It is important for all health-care professions to systematically develop and evaluate nutritional therapy for the elderly and the chronically ill.

Background

There is an extensive literature in the fields of geriatric and internal medicine which documents a strong connection between chronic illness-related malnutrition and increased morbidity, mortality and prolonged time in care. The causal relationships have not been clarified, however, which means that treatment with additional energy, nutrients and liquids does not necessarily improve the patient's health status or prognosis. Also, reduced food intake and the breakdown of body tissues partly result from biochemical mechanisms that are activated by illness. This raises additional questions about the potential for correcting illness-related malnutrition by increasing the supply of nutrients.

This chapter summarizes research on the effects of nutritional therapy for existing or potential malnutrition, especially in connection with chronic illnesses that are very often associated with the condition (see Table 1). The final stages of most chronic organic illnesses – especially those of the lungs, heart, nervous system, skeleton, kidneys and joints – are associated with both general and specific catabolic and hypermetabolic processes, as well as reduced intake of nutrients and liquids. This may lead to malnutrition in some patients. (For a discussion of gastrointestinal illnesses, including cirrhosis of the liver, see Part II, Chapter 7.)

Table 1. *Chronic medical conditions often associated with malnutrition.*

Chronic obstructive lung disease
Chronic heart disease
Aftermath of stroke
Dementia
Recovery from fractured hip
Chronic renal failure
Rheumatoid arthritis
Multiple illnesses in the elderly

The studies of treatment selected for this review are all concerned with treatment of general protein-energy malnutrition. In most cases, the treatment consisted of dietary supplements via drinkable liquids, or enriched foods which in some cases were administered via feeding tube. Some of the studies involve treatment with drugs such as growth hormone and anabolic steroids. To the greatest extent possible, randomized controlled trials (RCT) have been selected. However, that methodological foundation is lacking in many cases, and it has been necessary to include some less well-controlled studies.

In order to provide an overview, the most important results are summarized in tabular form, usually in reverse chronological order. Every section begins with background information on the prevalence of malnutrition, pathophysiological mechanisms, and the prognostic significance of malnutrition for various illnesses.

Methodological consideration

It turned out to be difficult to find literature in the medical data base, Medline, that provides a comprehensive description of nutritional therapy's effects. For example, only 69 original articles were found in the spring of 1998, using the OVID program to search under the following categories: "nutritional and metabolic diseases", "nutrition disorders", "wasting and starvation", and the combination of "diet therapy, drug therapy, nursing, rehabilitation, therapy". The searches were all in English and restricted to studies of individual adult humans.

There are several probable reasons for the meagre results. Among other things, Medline's indexing of articles on nutritional treatment is not uniform. For example, articles on the subject may be included under the headings of "intervention", "supplement" and "support". Treatment studies are often included in articles that also deal with epidemiological issues, diagnosis and prognosis. Further, some nutrition publications, such as the Nordic journal, *Näringsforskning*, are not indexed in Medline. Some have only recently started to be indexed, such as the *Journal of Human Dietetics and Nutrition* (from 1995) and (from 1998). This means that many Swedish and other treatment studies are not indexed in Medline.

The search program, PubMed, has also been used, including the function "see related articles". After repeated searches in Medline, partly with the help of our own and the expert panel's reference data, 65 references have been found which bear some relation to treatment of malnutrition in the chronically ill.

Chronic obstructive pulmonary disease

The rate of malnutrition in patients with various forms of chronic obstructive pulmonary disease (COPD) has been reported as varying between 20–70 percent; the highest rates are among those with emphysema (1, 2, 3).

COL-related malnutrition probably involves a combination of hypermetabolism due to increased breathing effort (4–7) and inflammatory catabolic activity (8–10). A recent study using double-indicator water found that average total energy use among COL patients was about twenty percent higher than in a matched control group (7). The baseline metabolic rate (BMR) was not elevated, but energy use among COL patients increased in connection with physical work and greater diet-induced thermogenesis. Another recent study, of COL patients during stable phases, found that BMR was related to plasma levels of tumour necrotic factor (TNF), but not to respiratory function (11).

Other factors which may contribute to malnutrition include adaptation to reduced physical activity, and treatment with systemic glucocortocoids. There has also been some discussion of the possibility that COL may develop as a result of hypermetabolism, anorexia and iatrogenic starvation in connection with acute stages of disease (5).

The loss of lean body mass in COL patients leads, among other things, to reduced diaphragm mass and to impaired function of the breathing muscles and peripheral skeletal muscles (1, 12). General muscle hypotrophy leads to general reductions of functional capacity. In COL patients with the same level of reduced lung function , body weight is negatively correlated with mortality (13). It has therefore been speculated that impaired lung function from emphysema may possibly be related to nutritional status (1, 14). As early as thirty years ago, it was reported that the five-year survival rate of COL patients with significant weight loss was lower than those without weight loss. After the onset of weight loss, the average survival time was three years (15).

Treatment (table 2)

Summarized in Table 2 are fourteen studies, including twelve based on RCT methodology (2, 16–28). Among the fourteen are four (including three RCT) which studied treatment with dietary supplements in combination with anabolic steroids or growth hormone (GH). There are also two non-controlled studies, and two on the effects of dietary supplements on COL patients who were not undernourished. With the exception of one study, the sample sizes were small (9–33 patients), and the treatment times ranged from two to 52 weeks.

Table 2. Studies of treatment for malnutrition in COL patients.

Authors	Year	Type	Patients			Treatment				Effects		
			No.	Mean age	Mal-nour-ished	Type	Energy (kcal/d)	Protein (g/d)	Time	Anthro-pometry/ Biochemistry	Function	Morta-lity
Ganzoni *et al.* (16)	1994	RCT	30		Yes	Special food	Energy ↑		52 wk	None	None (subj. ↑)	X
Rogers *et al.* (17)	1992	RCT	27	64	Yes	Special food ?	+ 0,3 x REE		16 wk	Weight ↑	Musc. strength ↑ (breathing, hand, walking)	X
Fuenzalida *et al.* (18)	1990	RCT	9	62	Yes	SUP	+ 1080	+ 43	3 wk	None	Immunity ↑	X
Whittaker *et al.* (19)	1990	RCT	10	71	Yes	Enteral NG	+ 1000	0	6 d	Weight ↑	Musc. strength ↑ (breathing)	X
Otte *et al.* (20)	1989	RCT	13	56	Yes	SUP	+ 400	+ 20	13 wk	Weight ↑ SC fat ↑	None	X
Efthimiou *et al.* (21)	1988	RCT	14	60	Yes	SUP	+ 690	+ 29	12 v	AM ↑ LBM ↑	Musc. strength ↑ (breathing, hand) AT ↑, walking ↑	X
Lewis *et al.* (22)	1987	RCT	21	65	Yes	SUP	+ 500–1000	+ 18	8 wk	None	None	X
Ferreira *et al.* (23)	1998	RCT	23	70	Yes	Testosteron			27 wk	AM	None	X
Burdet *et al.* (24)	1997	RCT	16	66	Yes	Special food + GH	40/kg/d		3 wk	LBM ↑	None	X
Schols *et al.* (25)	1995	RCT	217		Yes	SUP + Nandrolone	+ 420		8 wk	Weight ↑ (Special food ⇒fat ↑ Comb⇒LBM ↑)	Musc. strength ↑ (breathing)	X
Saudny-Unterberger *et al.* (26)	1997	RCT	33	69	No	SUP	+ 10/kg	+ 10	2 wk	X	Lung function ↑	X
Knowles *et al.* (27)	1988	RCT	25		No	SUP	+ 360–540	+ 21–32	8 wk	Weight ↑	None	X
Sridhar *et al.* (28)	1994	NC	9	66	Yes	SUP	+ 50 %	+ 1.5 g/kg	16 wk	None	None	X
Pape *et al.* (2)	1991	NC	7	63	Yes	Special food + GH	35/kg/d	1/kg/d	3 wk	Weight ↑ Nutr. balance ↑	Musc. strength ↑ (breathing)	X

Abbreviations: AM = anthropometric index, GH = growth hormone, LBM = lean body mass, NC = non-controlled, NG = nasogastric tube, RCT = randomized controlled trial, REE = resting energy expenditure, SC = subcutaneous, SUP = dietary supplement, X = not studied.

The main findings were as follows:

- 14 of 19 studies (8 RCT) found positive effects of treatment, based on various structural measures, primarily body weight.
- 14 of 17 studies (6 RCT) noted functional improvements in lung function, immune system function, or the strength of skeletal muscles (breathing and/or extremities).
- 14 of 15 studies (4 RCT) found positive effects, based on both structural and functional measures.
- 13 of 14 studies (2 RCT) found no effects of nutritional treatment.
- None of the studies evaluated effects on mortality or quality of life.
- Of the four studies involving treatment of COL patients with anabolic steroids or growth hormone (separately or in combination with dietary supplements) positive effects as measured by anthropometric indices were found in all four, and improved muscle function in two of the studies.
- Of the two studies involving treatment with dietary supplements to COL patients who were not undernourished, one found positive effects on lung function.

Conclusion

Many of the studies, but not all, found that nutritional treatment of malnutrition in cases of chronic obstructive lung disease can have positive effects on physical constitution and, in some cases, also on muscle strength and breathing function.

Chronic heart disease

Malnutrition in connection with serious, chronic heart disease (rating of 3–4 on New York Heart Association scale) is classified as heart cachexia (29–32). The reported rate of malnutrition varies between 10 and 25 percent, depend on the type of heart condition involved (33–37). The question of whether or not the increasing use of ACE inhibitor has reduced the risk of heart cachexia has not been studied.

Among the pathophysiological mechanisms of heart cachexia are reduced appetite, premature satiation, secondary portal hypertension with venous stasis in the liver and the splancnic area with dyspepsia, malabsorption of fat, and protein loss in the gut (32, 38–41). Recent years' research has found that cytokin-triggered catabolism contributes to heart cachexia (37, 42–44). The basal metabolism of older patients with chronic heart disease is about 15–20 percent higher than that of matched controls (40, 45). Possible causes are increased breathing effort or oxygen requirements of the myocardium. Systemic factors, e.g. increased activity of the sympathetic nervous system, may also contribute (46). Due to the lower level of physical activity, however, total daily energy use does not increase, as measured with the double-indicator water method (47).

Starvation leads to hypotrophy of the heart muscles, in proportion to hypotrophy of the skeletal musculature (48). In healthy individuals, this can be an adaptive response to lower metabolic demands (e.g. bradycardia, hypotension, reduced blood volume), which seldom leads to heart disease (39). It has been reported that undernourished patients with no clinical indication of heart disease may have EKG and FKG-like indications of subclinical left-chamber dysfunction which can be reversed with nutritional therapy (49). Nutritional treatment of starvation involves a risk of heart disease, especially when nutrition is supplied parenterally; this is the so-called refeeding syndrome (32, 39). There is a correlation between heart disease and excess mortality (50–52).

Treatment (table 3)

One non-controlled study has investigated the effects of nutritional treatment on five patients with both chronic heart disease and malnutrition (53). There is also a Swedish RCT study of the effects of nutritional treatment for chronic heart disease in patients who were adequately nourished (36), and another Swedish study of nutritional treatment and heart function in patients with healthy hearts but multiple diagnoses for other types of illness (48). These studies were limited in scope, however, and no negative effects of nutritional treatment, e.g. volume overload, were found.

Nutritional treatment of heart disease is complicated by the fact that patients' daily liquid and saline intake should not exceed 1.5 litres or 2 g sodium, respectively. Therefore, heart cachexia often requires highly-concentrated energy and restricted sodium intake (41, 54). A schedule of frequent meals may be preferable to a smaller number of heavy meals.

Conclusion

Nutritional treatment of malnutrition in cases of chronic heart disease has not been adequately studied.

Table 3. *Studies of treatment for malnutrition in patients with chronic heart disease.*

Authors	Year	Type	Patients				Nutritionsbehandling				Effekter		
			No.	Mean age	Diag-nosis	Mal-nutri-tion	Typ	Energy (kcal/d)	Protein (g/d)	Time	Antropo-metric/Bio-chemical	Function	Morta-lity
Heymsfield *et al.,* (48)	1978	NC	5	49	Mul-tiple; healthy heart	Yes	Enteral Parent	3000–4000	75–135	2–5 v	Weight ↑ LBM ↑	Heart ↑	X
Heymsfield *et al.,* (53)	1989	Hist. NC	4	55	Heart disease NHA 3–4	Yes	Enteral	35/kg	1.0/kg	2 v	Weight ↓ LBM ↑	None	X
Broqvist *et al.,* (36)	1994	RCT	22	65	Heart disease NHA 3–4	No	SUP	+ 750	+ 30	8 v	SC fat ↑	None	X

Abbreviations: AM = anthropometric index, GH = growth hormone, LBM = lean body mass, NC = non-controlled, NG = nasogastric tube, RCT = randomized controlled trial, REE = resting energy expenditure, SC = subcutaneous, SUP = dietary supplement, X = not studied.

Stroke aftermath

Among victims of stroke, 8–16 percent show signs of malnutrition from the onset of illness (55–57). Within one week of stroke, about one-third of the victims need help with feeding and their nutritional status steadily declines (56).

A Swedish study of stroke patients found that the rate of malnutrition increased from 16 percent at admission to 22 percent upon discharge (55). The corresponding figures in a Spanish study were 16 percent and 26 percent after one week (57). Over eighty percent of stroke patients hospitalized for more than 21 days had problems with eating (58). Nearly half of the patients referred to one stroke rehabilitation clinic were undernourished (59).

Much of the functional impairment associated with stroke has an effect on the invalid's ability to maintain adequate nutrition. Difficulty in swallowing, dysphagia, affects 30–45 of victims (60–61). Half of them have recovered the ability to swallow after one week, and the great majority (87 percent) have done so after two weeks (60, 62). At present, there is uncertainty about the point in time at which dysphagia in a patient should be regarded as permanent. This uncertainty often leads to delays in supplying nutrition to stroke/dysphagia victims, in anticipation of spontaneous improvement.

This tendency to avoid nutritional treatment is strengthened by a lack of guidelines based on the results of controlled studies (63). Other factors that may contribute to the risk of malnutrition after stroke include paresis of the body's dominant side, communication and perceptual disturbances such as aphasia, and impairment of the taste and smell senses. Davalos *et al.* have speculated that catabolic processes in the acute phase, expressed as heightened cortisol levels in urine and plasma, may contribute to a negative energy-nutrient balance which can rapidly worsen nutritional status in many stroke patients (57).

Malnutrition in stroke patients is associated with increased rates of infection, bedsores, prolonged time in care and increased mortality (57, 64). As with many other conditions, hypoalbuminemia is an especially strong indicator of poor prognosis (65).

Treatment (table 4)

Table 4 summarizes six studies, including two using RCT methodology (57, 66–70). The studies dealt with various types of nutritional treatment, all of which focused on prevention of malnutrition following a stroke. One study found that oral dietary supplements lead to increased nutrient intake and less pronounced deterioration of nutritional status (66). Another, non-controlled, short-term study found that gastronasal feeding did not hinder the deterioration of nutritional status (57).

Table 4. *Studies of nutritional treatment of stroke patients.*

Authors	Year	Type	Patients		Treatment				Effects	
			No.	Dysphagia	Type	Energy	Protein	Time	Anthropometry/Biochemistry	Function/Mortality
Gariballa *et al.,* (66)	1998	RCT	40	No	Oral SUP	+600 kcal	+20 g	4 wk	Increased intake of energy (75%) and protein (50%). Lower S-albumin in control group	
Norton *et al.,* (67)	1996	RCT	30	Yes	PEG or NG 14 days after onset of illness	100 ml/hr. NG		6 wk	Weight and s-albumin rose in PEG-gruppen. Both variables declined in NG group	Lower mortality, shorter care time, fewer complications in PEG group
Davalos *et al.,* (57)	1996	NC.	91	Yes & no	Normal food (oral) or, if dysphagic, enteral nutrition via NG	2000 kcal (oralt) alt. 30 kcal/kg (NG)	16 g (oral) 14 g (NG)	1 wk	Those with low TSF, AMC or salbumin increased from 17% to 32% despite treatment	
Wanklyn *et al.,* (68)	1995	Retro-spective	37	Yes?	PEG 26 days (median) after onset of illness					25 of 37 patients died within three months
Nyswonger *et al.,* (69)	1992	Retro-spective	20/32		Enteral nutrition (NG) before and after 72 hrs. from onset of illness					20 days in care with early treatment; 29 days if later
Elmståhl *et al.,* (70)	1999	NC	38	Yes	Mouth-muscle training; training in swallowing and body position					60% improved swallow function and nutrtional status

Abbreviations: AMC = arm muscle circumference, NC = non-controlled, NG = nasogastric tube, PEG = percutaneous endoscopic gastrostomy, RCT = randomized controlled trial, SUP = dietary supplement, TSF = triceps skinfold.

One RCT study compared percutaneous endoscopic gastrostomy (PEG) with the nasogastric feeding tube method (67). In the latter case, patients with severe stroke and persistent dysphagia received 100 ml/hour standard solution via feeding tube. Mortality was lower in the PEG group – twelve percent, compared with 57 percent among those fed nasogastrically. In addition, time in care was briefer, complications from aspiration pneumonia were fewer, and nutritional status was better in the PEG group.

A retrospective of long-term study of effects on stroke patients who received PEG found that 25 of 37 patients had died within three months of stroke (68). It was not possible to evaluate the extent to which this poor outcome resulted from inadequate nutrient intake prior to treatment with PEG. A non-controlled Swedish study has found that training the swallowing function and adjustments in diet improved swallowing and nutritional status in a majority of dysphagic stroke patients (70). In a review and analysis of the literature on treatment of dysphagia in victims of severe stroke, the Cochrane Library concluded that far too few studies had been conducted. It is possible that PEG can improve function and nutritional status in stroke patients more effectively than the nasogastric method.

Conclusion

Nutritional therapy for the effects of stroke has not been adequately studied. In cases of permanent dysphagia, treatment with percutaneous endoscopic gastrostomy circa fourteen days after the onset of illness may be preferable to the nasogastric feeding tube method.

Dementia

Malnutrition occurs among 12–50 percent of those institutionalized with dementia (72–74). The rate for dementia of Alzheimer type, DAT, has been reported to be higher than for vascular dementia (75). Within eight years of DAT's onset, fifty percent of those affected needed artificial nourishment or assistance with feeding (76). This raises important ethical issues (77).

There is a demonstrated relationship between weight loss and time spent in an institution, especially with DAT and even in patients whose food intake has been adequate (72–73). One retrospective longitudinal study of ten DAT patients fund an average weight loss of circa five kg/year following institutionalization (72). But dementia patients who are able to remain at home do not display any weight loss, according to other research (73, 78). This may be due to the fact that the amount of time allocated to meals is often longer in the home than in institutions (79). Another report has noted that the development of dementia may be preceded by involuntary weight loss of 3–4 kg within ten years, and the authors discuss the possibility that weight loss may be part of an early stage of dementia (80).

Dementia leads to lower energy intake, due among other things to reduced appetite/hunger/thirst, impaired eating function (e.g. chewing and swallowing), altered senses of smell and taste, and refusal or neglect to eat. Alzheimer patients may often experience increased energy loss due to hyperactivity, and there is some evidence that daily energy use in some patients can increase by as much as 1,600 kcal (81).

Controlled studies of DAT patients using indirect calorimetry have found both unchanged and increased basal metabolism (82, 83). A study of energy balance in DAT patients using double-indicator water was unable to find any evidence of hypermetabolism (84). Reference has been made to the so-called "sundown syndrome", a decline in the cognitive ability of DAT patients during the evening, due to fatigue caused by hyperactivity during the day (85).

It is likely that inflammatory processes in the brain are significantly related to the development of DAT (86–87). Patients with DAT show signs of ongoing brain inflammation, both local and systemic; among the indications are heightened levels of TNFa (88–90). The question arises as to whether this may contribute to weight loss. There are also indications that DAT patients experience a general deterioration of homeostatic regulatory mechanisms, such as those for body temperature and cardiovascular reflexes, which may lower the capacity to conserve energy (91).

A six-year longitudinal study found that weight loss was correlated with mortality and to the severity and progression of DAT, while weight gain lowered the risk of death (92).

Treatment

One study of nutritional therapy for patients with dementia and malnutrition at a psychiatric hospital in England found that, of 300 patients, 80 (27 percent) were underweight (74). Of these, 46 were included in a randomized controlled study of treatment with liquid dietary supplements of 600 kcal per day for twelve weeks. This resulted in an average weight increase of 3.5 kilograms, while the average weight of the control group remained unchanged. No evaluation of function or mortality was included in the study.

A retrospective study of nursing home residents with severe cognitive dysfunction found no effects of nasogastric feeding on survival rates (93). Especially in advanced stages of dementia, it is important to consider the ethical aspects of artificial nutrition.

Conclusion

Treatment of dementia-related malnutrition has not been adequately studied.

Rehabilitation after hip fracture

Roughly fifty percent of all older persons who suffer hip fractures are undernourished (94–97). Inadequate nutritional intake may contribute to the development of osteoporosis, which is often a precondition of fractures in the elderly. Malnutrition is also associated with muscle weakness which leads to increased risk of falling, and with reduced amounts of shock-absorbing subcutaneous fat (98, 99). Prospective long-term epidemiological studies have found that maintaining body weight after menopause is a significant factor in the prevention of fractures (100).

The combination of fractures, trauma from falls and surgical intervention often leads to intense inflammation that contributes to catabolic conditions in pre- and post-operative phases. The metabolic and nutritional consequences during these phases are discussed in Part II, Chapter 8.

One study of malnutrition's prognosticative significance for hip-fracture patients found that the risk of malnutrition was correlated with longer times in hospital and lower levels of rehabilitation (95).

Treatment (table 5)

Table 5 summarizes seven RCT studies of nutritional treatment of hip-fracture patients during the post-operative rehabilitation phase (101–107). All of the studies were controlled and randomized; but the randomization procedure is not clearly described in every case. Two of the studies involving dietary supplements were controlled with the use of placebos.

Four of the six studies of dietary supplements found that they led to less time in hospital. Two of six by the same research group found fewer post-operative complications such as infection. One of these six studies found significantly lower mortality; but the sample was very small, and a single death in the experimental group probably would have nullified that finding. One of the studies found that four weeks' treatment with anabolic steroids (nandrolone) had no positive effect.

A review and analysis by the Cochrane Group, of research involving a total of 943 patients above age 65, concluded that there was no evidence of positive effects from treatment with oral protein-energy supplements. However, the general quality of the studies was judged to be low and additional studies were recommended.

Conclusion

Nutritional treatment following hip fracture in the elderly may have positive effects. Available studies indicate that time in hospital can be reduced by oral or enteral treatment with enriched dietary supplements containing 20 grams or more of protein per day for at least three-four weeks during the post-operative phase.

Table 5. *Studies of nutritional treatment of hip-fracture patients.*

Authors	Year	Type	Patients		Treatment				Effects	
			No.	PEM	Type	Energy/d	Protein/d	Time	Anthropometry/ Bio-chemistry	Function/Mortality
Schurch *et al.,* (101)	1998	RCT, placebo	82	No	Oral SUP	–	+20 g	6 mo	Bone density and IGF-1 increased	Shorter time in hospital under 1 year: 33 vs. 54 days
Sullivan *et al.,* (102)	1998	RCT	18	No	Nightly NG feeding	+1400 ml		~15 d		Lower 6-month mortality, 0 vs. 50%
Tkatch *et al.,* (103)	1992	RCT, placebo	62	No	Oral SUP	–	+20 g	38 d		Lower mortality, fewer complications. Shorter care times under 7 mo.:
Delmi *et al.,* (104)	1990	RCT	59	No	Oral SUP	+250	+20 g	1 mo		Fewer complications. Shorter care times:
Williams *et al.,* (105)	1989	RCT?	28	Yes	Oral SUP	+~400 kcal	+14 g	~3 wk	TSC and AMC unchanged in exper. group; declined in control group	
Bastow *et al.,* (106)	1983	RCT	122	Yes	Nightly NG feeding	+1000 kcal	+28 g	~4 wk	AMC rose	Faster rehab.: 10 vs. 12 days ("thin") and 16 vs. 23 days ("very thin")
Sloan *et al.,* (107)	1992	RCT, placebo	29	No	Nandrolone 2 mg/kg intravenously	–	–	4 wk	Neither positive nor negative	

Abbreviations: AMC = arm muscle circumference, IGF-1 = Insulin-like growth factor 1, NG = nasogastric tube, PEM = protein-energy malnutrition, RCT = randomized controlled trial, SUP = dietary supplement, TSF = triceps skinfold.

Chronic renal failure

Malnutrition in connection with renal failure often becomes clinically detectable at GFR < 10 ml/min, and occurs with both conservative and active treatment for uraemia (GFR = glomerular filtration rate). The rate of malnutrition can be as high as 40–76 percent, and is especially common among older patients (109–111). It has been stated that undernourishment is very common with chronic renal failure that is ancillary to diabetes mellitus (112). Of 224 ambulatory patients with a mean age of 53 who underwent peritoneal dialysis (PD) for an average of 32 months, 41 percent were assessed as undernourished, and eight percent of these were extremely undernourished, according to SGA measurements (110).

Uraemia-related malnutrition is related to a combination of nutritional, metabolic, hormonal and inflammatory factors. The development of renal failure is often accompanied by gradual anorexia with spontaneous reduction of protein intake, independent of any diet counselling that may be offered (113). At GFR <10 ml/min, protein intake is often spontaneously reduced to < 0.6 g/kg per day (112). With careful diet counselling emphasizing increased energy intake, it has been possible to prescribe lower-protein food without the emergence of malnutrition (114). For many patients, however, the risk of malnutrition is great.

The activity of proinflammatory cytokins with anorectic and muscle-catabolic effects is heightened in cases of renal failure, and is associated with the development of malnutrition (115). Metabolic acidosis may contribute to muscle proteolysis and reduce albumen synthesis (116, 117). However, it is not clear whether it is possible to impede the development of malnutrition by treatment for metabolic acidosis (112).

Among the other factors that may contribute to disturbances to nutritional balance that are related to chronic renal failure are insulin resistance, increased concentrations of glucagon, secondary hyperparathyroidism, and reduced levels of thyroid hormones. To these factors may be added other potential co-morbid conditions such as diabetes mellitus, depression, drug side effects and physical inactivity. Several studies have reported that energy use in cases of chronic renal failure, with or without hemodialysis or continous peritoneal dialysis (CAPD)was the same as in healthy control subjects (118–120). But there are also studies that indicate increased energy use in cases of renal failure.

Variables that indicate malnutrition reflect strong risk-factors for both morbidity and mortality in connection with chronic dialysis (122, 123). There is also evidence that existing malnutrition, in itself, may have a negative effect on kidney function (124).

Treatment (table 6)

Table 6 summarizes eleven studies, three using RCT methodology (125–135). The sample sizes of the studies were small, ranging from 7–50 patients, and treatment time lasted from seven days to twelve months. Some studies involved treatment with a combination of food/supplements and growth hormone, a method that has been reported to improve nitrogen balance and reduce serum urea levels, without affecting muscle function (133). The question of whether or not four weeks is too short a treatment time was also discussed.

Nine of ten studies, including two of RCT type, found positive effects on the basis of various anthropometric and biochemical indices. Function was measured in only two studies.

To maintain a positive nitrogen balance in cases of chronic renal failure, with or without hemodialysis or CAPD, an energy supply of 35–38 kcal/kg is needed. There are no studies of energy or protein requirements in older dialysis patients (122).

For patients who cannot tolerate oral or enteral feeding, there are alternative methods for use with dialysis. It is possible to compensate for inadequate protein intake by supplying a high protein:energy ratio with intradialytic parenteral nutrition (IDPN), i.e. intravenous supplements of glucose, amino acids and/or fat administered in connection with dialysis (136). However, there are no published RCT studies of the effects of IDPN on malnutrition with chronic renal failure.

The few studies that do exist have shown a slight positive effect on biochemical nutrition indicators, and improvements in immunologic function (126, 132, 135). One non-randomized controlled study found that IDPN led to higher survival rates, but only in cases of severely impaired kidney function (126). A retrospective study of the same issue found that IDPN improved the survival rate of patients with chronic renal failure and malnutrition (127).

Another method for supplying nutrition in connection with dialysis is intraperitoneal nutrition (IPN) with solutions based on amino acids. No controlled study of treatment with IPN has been found.

Conclusion

Treatment of malnutrition associated with renal failure has not been adequately studied. Available research suggests that positive effects can be obtained for anthropometric and biochemical variables.

Table 6. Studies of treatment for malnutrition in patients with chronic renal failure.

Authors	Year	Type	Patients				Treatment				Effects		
			No.	Age	Dialysis	Mal nutrition	Type	Energy (kcal/d)	Protein (g/d)	Time	Anthropometry/ Biochemistry	Function	Mortality
Tietze *et al.,* (125)	1991	RCT	19	55	HD	Yes	SUP (fish prot.)	32 kcal/ kg/d	+ 8	3 mo	Anthropom ↑, Weight ↑, muscle ↑, protein profile ↑	X	X
Chertow *et al.,* (126)	1994	Non-rand. control			HD		IDPN			12 mo	S-albumin ↑	X	↓ if s-alb. <35, S-krea <700 ↑ if s-alb. >35
Capelli *et al.,* (127)	1994	Retro. non-rand. control	50	60	HD	Yes	IDPN	+670–725 kcal/ dialysis	75–100g/ dialysis	9 mo	Weight ↑, Fat mass ↑	X	↓
Hecking *et al.,* (128)	1978	Non-rand. control	13	41	HD	Yes (?)	EAA	+ 60	+ 15,7	3 mo	None	X	X
Milano *et al.,* (129)	1998	NC	22	43	HD	Yes	SUP	+ 380	0	6 mo	Antropom ↑, fat mass ↑	X	X
Elias *et al.,* (130)	1989	NC	8	49–78	PD	Not stated	SUP	+ 80	+ 15	4 mo	Nutr. balance ↑	X	X
Acchiardo *et al.,* (131)	1982	NC	15		HD	Yes	Ess. tot. prot-ein profile+ Energy	35 kcal/kg/d	1		S-tot-prot ↑, S-albumin ↑, S-transferin ↑, TLC ↑, Bone density ↑		
Johannson *et al.*, (132)	1999	RCT	17	73	HD	No	GH			6 mo	Fat free mass ↑, S-IGF-1 ↑, S-albumin ↑	Mobility ↑, HK ↑	
Iglesias *et al.,* (133)	1998	RCT	8	64	HD/PD	Yes	GH	Special food	Special food	4 wk	Weight ↑, S-IGF ↑, S-transferin ↑, S-urea ↑	None	X
Ikizler *et al.,* (134)	1994	NC	10	46	PD	No	GH	–	stable	7 d	S-IGF ↑, S-albumin ↓	X	X
Schulman *et al.,* (135)	1993	NC	7	48	HD	Yes	IDPN + GH	+18 kcal/ kg/dialysis	+0,69 g/ kg/dialysis	6 wk	N-balance ↑, S-albumin ↑, S-transferin ↑	X	X

Abbreviations: EAA = essential amino acids, GH = growth hormone, HD = hemodialysis, HK = hand strength, IDPN = intradialytic parenteral nutrition, IGF-1 = insulin-like growth factor 1, NC = non-controlled, PD = peritoneal dialysis, RCT = randomized controlled trial, SUP = dietary supplement, TLC = total lymphocyte count, X = not studied.

Rheumatoid arthritis

Reported rates of malnutrition in connection with rheumatoid arthritis (RA) range from 26–71 percent (138, 139). It has been noted that RA patients seldom have reduced appetite, and that they can be in a definite state of malnutrition without this being detected by clinical examination (140). In one study of individuals with RA, only a few were diagnosed as undernourished (141).

RA implies a risk of malnutrition for several reasons. Patients with RA lose muscle mass, even with high protein intake (142). This is consistent with the catabolic processes that are linked to the chronic inflammation of RA, which is in turn consistent with findings of increased system TNF-α activity associated with the development of RA-related malnutrition (140, 142).

Distinct radiological changes, extra-articular manifestations and low functional capacity are all strong indicators of malnutrition with RA (138, 143). There is often weight loss during the active phase of the illness (144). New treatment strategies targeted directly a TNF-α activity are starting to be applied to RA (145, 146). What effects this may have on general illness-related catabolism are not yet known.

Other factors that may possibly contribute to malnutrition are adaptation to reduced physical activity, and treatment with systemic glucocorticoids. Secondary Sjögren's syndrome, including dry mouth, is relatively common with RA. Also, there may be some risk of malnutrition associated with repeated periods of fasting or laxative diet for the purpose of lowering illness activity.

Conclusion

The treatment of malnutrition in connection with rheumatoid arthritis has not been studied.

Treatment

There are no published studies on the effects of nutritional treatment of malnutrition in connection with rheumatoid arthritis.

Multiple illnesses in older patients

The combination of old age, multiple chronic illnesses and polypharmacy implies an increased risk for malnutrition (34–35, 147–150). A Swedish study of internal-medicine patients found that the rate of malnutrition among those above age 74 was twice that of those aged 65–74, i.e. 27 vs. 13 percent (35). In connection with an ongoing evaluation of a major reform of old-age care by the National Board of Health and Welfare, it has been reported that malnutrition as defined by the MNA method (see Part I, Chapter 2) is very common in Swedish old-age care (151–153).

Within geriatric and old-age care, it is often difficult to link malnutrition to any definite illness-related process. The degenerative processes of ageing often lead to reduced reserve capacity in several organs. Further, older patients often have several illnesses in various organic systems at the same time. This means that the pathophysiological mechanisms of isolated illnesses referred to above may interact in various ways, increasing the risk of malnutrition in older persons.

A number of studies have found evidence that malnutrition and underweight (especially in connection with ongoing weight loss) sharply increase the risk of mortality among the elderly and the chronically ill (51, 154–163). A retrospective study of undernourished older nursing home patients found that individuals whose weight increased by five percent or more during roughly one year experienced lower mortality, compared with those whose weight declined or remained unchanged (164).

Treatment (table 7)

Table 7 summarizes 23 studies of treatment, including thirteen using RCT methodology (165–187). Most of the studies involved orally administered liquid dietary supplements. The study periods ranged from two weeks to six months, and the number of patients from 12 to 435.

Eighteen of the studies (10 RCT) noted a rise in anthropometric and/or biochemical measurements in the experimental group. Ten studies (5 RCT) observed functional improvements. One RCT study reported that dietary supplements reduced the number of fall-trauma incidents (172). In one Swedish study, nutritional treatment administered to the adequately nourished control group was associated with both reduced mortality and increased general function; but no such effect was observed among the undernourished subjects (172).

We have found one study that evaluated the effects of treatment in undernourished older patients with intravenous nutrition. Sixteen moderately undernourished patients (average age 68) were randomly distributed into a group that received total parenteral nutrition (TPN) and a control group. It was found that protein synthesis was stimulated if energy supply from carbohydrates and fat corresponded to 200 percent of basal metabolism (188). We have not found any study which examined the effects of adjuvant parenteral nutrition, often administered to hospitalized older patients.

Conclusion

Some studies, but not all, have fund that nutritional treatment for malnutrition in older patients with multiple illnesses may have positive effects, primarily on physical constitution, and in some case also on muscle strength and immunologic function.

Table 7. *Studies of treatment for malnutrition in older persons with multiple illnesses.*

Authors	Year	Type	Patients			Treatment				Effects		
			No.	Age	Mal nutrition	Type	Energy (kcal/d)	Protein (g/d)	Time	Anthropometry Biochemistry	Function	Mortality
Fiatarone Singh *et al.,* (165)	2000	RCT	50	85	No	Nutr. drink	+ 360		10 wk	Weight ↑, fat ↑, FFM ↑	None	X
Laque *et al.,* (166)	2000	RCT	78	85	Yes/No	Nutr. drink	+ 400			Weight ↑ in undernourished	MNA ↑, None on hand strength	X
Bourdel-Marchasson *et al.,* (167)	2000	RCT	672	83	Yes/No	Nutr. drink	+ 400		15 d	X	Risk of bedsores ↓	X
De Jong *et al.,* (168)	1999	RCT	145	78	Yes/No	Enriched food				Vitamin status ↑, else none	X	X
McWhirter *et al.,* (169)	1996	RCT	86	72	Yes	Nutr. drink (enteral)	+ 590 + 640	+ 22 + 24	10 d 12 d	Weight ↑	X	X
Volkert *et al.,* (170)	1996	RCT	46	85	Yes	Nutr. drink	+ 250		6 mo	None	ADL ↑, Independence ↑	X
Hogarth *et al.,* (171)	1996	RCT	87	83	No	Glucose and/ or multivit.	+ 540	0	30 d	None	X	X
Gray-Donald *et al.,* (172)	1995	RCT	50	78	No	Nutr. drink	+ 150	+ 5	12 wk	Weight ↑	No. cases ↓	X
Fiatarone *et al.,* (173)	1994	RCT	100	87	No	Nutr. drink + training	+ 360	+ 15	10 wk	Weight ↑	None	X
Hankey *et al.,* (174)	1993	RCT	14	81	No	SUP + glucose-polymer	> 1000		8 wk	TSF ↑ AMC ↑	X	X
Unosson *et al.,* (175) Larsson *et al.,* (176)	1992 1990	RCT	435	79	28 % of group	Nutr. drink	+ 400	+ 16	26 wk	Weightindex ↑ AMC ↑, but only for well-nourished S-prealb ↑	Activity ↑ mainly for the well-nourished Skin test ↑ for both under- and well-nourished	↓ Only for well-nourished

Table 7. *Continued.*

Authors	Year	Type	Patients			Treatment				Effects		
			No.	Age	Mal nutrition	Type	Energy (kcal/d)	Protein (g/d)	Time	Anthropometry Biochemistry	Function	Mortality
McEvoy *et al.,* (177)	1982	RCT	51	–	Yes	SUP	+ 644	+ 36	4 wk	Weight ↑ TSF ↑	X	X
Banerjee *et al.,* (178)	1978	RCT	50	81	No	Nutr. drink	+ 265 (eg + 0)	+ 11	14 wk	Skin fold ↑ Skin status ↑	X	X
Bos *et al.,* (179)	2000	CNR	23	80	Yes	Nutr. drink	+ 1,67 MJ	+ 30	10 d	Proteinsynthesis ↑, fat free mass ↑	X	X
Ödlund-Olin *et al.,* (180)	1996	CNR	36	82	No	Enriched food	+ 450	+ 17	6 wk	Weight ↑	Physical aktivity ↑	X
Cederholm *et al.,* (181)	1995	CNR	23	74	Yes	Nutr. drink (Fortimel)	+ 400	+ 40	12 wk	Weight ↑, AMC ↑ TSF ↑	Musc. strength ↑ (hand), Skin test ↑	X
Hébuterne *et al.,* (182)	1995	NC	46	77	Yes	Enteral (Ventricular tube)	+ 1300	+ 68	2–6 wk	Weight ↑, TSF ↑, AMC ↑, S-prealb ↑	X	X
Gray-Donald *et al.,* (183)	1994	NC	14	–	No	Nutr. drink	+ 390		12 wk	Weight ↑	Musc. strength ↑ (hand) Wellbeing ↑	X
Elmståhl *et al.,* (184)	1987	NC	28	85	No	Nutr. drink (3 diff.)	+ 500 (eg. + 250–400)	+ 1–4	8 wk	Weight ↑	X	X
Lipschitz *et al.,* (185)	1985	NC	12	75	Yes	Nutr. drink	+ 815	+ 30	16 wk	Weight ↑, S-albumin ↑ S-TIBC ↑	X	X
Katakity *et al.,* (186)	1983	NC	12	77	No	Nutr. drink	+ 204	+ 9	12 wk	X	Musc. strength ↑ (hand)	X
Lipschitz & Mitchell (187)	1982	NC	9	75	Yes	Nutr. drink/ (Ventricular tube enteral)	1800–2500		21 d	Weight ↑ S-albumin ↑, S-TIBC ↑	Mobility ↑	X

Discussion

Basic vs. "medical" nutrition

As far as possible, recommendations for treatment should be based on the results of randomized controlled trials (RCT). But in some respects, nutritional treatment is an exception to that scientific rule. An adequate supply of nutrition is undeniably a precondition for the continuation of life in both healthy and unhealthy individuals, and there is no need for randomized studies to confirm this.

However, questions do arise concerning appropriate methods for administering and evaluating treatment for potential or established malnutrition. Apart from maintaining basic life-sustaining functions, nutritional treatment may also have "medical" significance.

Illness-related malnutrition is usually caused by the illness, itself, which can activate biochemical and physiological mechanisms that affect appetite, the structure of body tissues, and the ability of metabolic systems to process energy and nutrients. Such pathophysiological changes may be an adaptive and homeostatic.

As previously noted in this review of the literature, the current state of knowledge is in most cases inadequate to provide a solid scientific basis for guidelines and recommendations concerning the design of nutritional treatment.

Methodological problems

It should be underlined that there are substantial methodological problems associated with the execution of randomized controlled studies of treatment, and with the interpretation and comparison of results. Definitions of malnutrition vary between studies, reflecting the fact that there is no generally accepted definition of the concept (see Part I, Chapter 2).

The interpretation of results is also complicated by the diversity of treatment methods, uncertainty as to whether the specified treatment has been properly carried out, the simultaneous application of other interacting measures, small and often heterogeneous samples, short treatment times, and lack of clinically relevant outcome variables. It should also be noted that malnutrition usually occurs together with chronic illnesses and catabolic processes whose natural courses are difficult to control. Positive effects may be difficult to detect in the typically complex situations of nutritional treatment.

In addition, the results of treatment are usually studied only at the group level. Thus, there is a great risk that positive effects among certain subgroups may not be observed, given that there are often wide variations in energy intake by the same individual and between different individuals.

Structure & function

An important question to consider is the significance of treatment-induced increases in the values of anthropometric and/or biochemical variables. Weight loss and hypoalbuminemia are both strongly correlated with increased mortality of invalids. Since the causal relationships are often unclear, there is no guarantee that patients' functional capacity, prognosis or quality of life will improve as a result of nutritional treatment that increases the value of anthropometric variables such as body weight, or biochemical variables such as serum albumin.

Several studies have found that balanced nutritional treatment can influence physical constitution according to the following sequence: First, total body water increases, then fat, and finally lean body mass, i.e. muscle and protein (191, 192). An important objective of nutritional treatment is to restore lean body mass. However, many of the studies reviewed have found that nutritional treatment leads primarily to increased storage of fat. It is unclear whether this finding is of minor clinical relevance, or points to an indirect indicator of simultaneous anabolic muscular processes. On the other hand, improvements of clinical function need not be related to increased body weight, since nutritional treatment can more rapidly affect an organ's function than its size and mass (193).

The possibility cannot be excluded that an optimal supply of nutrition, provided by the means available today, has only a limited potential to improve the health of undernourished patients – especially if the condition is related to catabolic processes and increased energy use, rather than to reduced energy-protein intake. Physical training and pharmacological measures, both anabolic and anti-catabolic, may come to serve as supplementary treatment methods, for example to promote muscle growth. Studies in this area are currently in progress.

A potential weakness of most treatment studies is that total energy intake can seldom be reported. Nutritional treatment usually involves an additional 200–500 kcal of energy per day, which does not necessarily lead to a corresponding increase in total intake. Treatment with dietary supplements may suppress appetite and reduce intake of the normal diet (22, 27, 173, 184). Older patients vary in their ability to follow instructions for dietary supplements (171, 174). Large doses of liquid supplements have been reported to produce bloating and gas formation as side effects (22). But many studies have found that supplements or enrichment can increase total energy intake (66, 166, 169, 170, 180, 194).

Fat quality

Another uncertain factor is the extent to which the additional supply of fat has any effect on health, other than serving as a concentrated source of energy. At present, enriching the energy quotient of meals is usually achieved with additions of saturated fatty acids in the form of dairy products. The question of whether this leads to negative effects, such as increased thrombogen activity, needs to be investigated.

Research on standard health care

As a rule, treatment studies are conducted by specialized research groups under standardized conditions. Consequently, the results of that research cannot be applied to standard health-care treatment without reservation. This is illustrated by a six-month study of the routine administration and evaluation of artificial nutrition in a Scottish teaching hospital. The researchers found that prescriptions for nutritional treatment were neither adequate nor administered to patients according to prescription, and concluded that the supply of nutrition was insufficient (148).

In another example, a retrospective study of nursing homes found that dietary supplements were used as non-specific treatment for weight loss, without regard to diagnosis of underlying causes, and with no documentation of the amounts consumed or the outcome of treatment (195). Such findings underline the need to increase care personnel's knowledge and awareness of nutrition's significance, through education and the improvement of procedures.

Conclusion

A total of 65 studies of nutritional treatment (32 RCT) have been reviewed, the majority of which involved orally administered liquid dietary supplements. Mortality benefits were noted in five of the studies (eight percent), functional improvements in 23 (35 percent), and anthropometric/biochemical improvements in 42 (65 percent). Six studies (nine percent) with control groups found no improvements. In no study were serious side effects observed.

Even though there are many uncertain factors relating to the reviewed studies, the available data indicate that dietary supplements, in the form of balanced-liquid or protein-rich drinks, can yield positive results in patients with existing or potential malnutrition connected with certain chronic illnesses.

A similar conclusion was reached by a recently published review and analysis of 32 studies involving a total of 2286 randomized patients who received dietary supplements orally or enteralally (196). There was no indication that the advantages of treatment were limited to special diagnostic groups. The most positive results of treatment have been reported for undernourished patients with chronic obstructive lung disease (improved breathing function), older women recovering from hip fractures (accelerated rehabilitation and correspondingly shorter time in care), and adequately nourished older persons with multiple illnesses (increased functional capacity).

However, the literature is not conclusive, and there is a lack of treatment studies for certain types of illness. The same general conclusion is drawn in two recently published articles (197, 198).

In accordance with the above-noted reviews and analyses, the authors also conclude that there is a great need for additional randomized, controlled long-term studies, preferably with the use of placebos, into the effects of structured programmes for the treatment of single and multiple illnesses in older patients. Apart from measuring the values of anthropometric and biochemical outcome variables, attention should be focused on clinically relevant measures of function such as morbidity, functional capacity, health-related quality of life, time in care and mortality.

There is an additional need for experimental studies and randomized treatment studies, in order to develop improved methods of treatment to impede catabolic processes while stimulating appetite and anabolic processes. It is also urgent to focus research on the development of nutritional treatment programmes that are integrated with other types of clinical treatment, and on the effects of long-term treatment in the patient's home environment.

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