
Weight Loss in Alzheimer's Disease

Alzheimer's disease (AD) is an increasingly prevalent health problem, with many associated challenges and comorbidities. Unexplained weight loss is a frequent clinical finding, and is linked to numerous risk factors, which often raise more questions than answers. Current interventions also appear questionable, however, clinicians still have beneficial treatment options and, most importantly, play a major role in answering questions from the AD patient's family and reassuring the family about the care being given to their loved one.

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Weight loss can precede the clinical diagnosis of Alzheimer's disease (AD),^{1,2} especially as competency in instrumental activities of daily living (IADL) declines. More commonly, however, weight loss is associated with more severe disease and becomes more likely, and more marked, as the disease progresses.^{3,4} Weight loss and malnutrition increase the risk of infection and skin ulcers, and are associated with falls and decreased quality of life.⁵ Weight loss in AD may be a predictor of mortality and, conversely, weight gain has been associated with longer survival and a slower progression of disease.⁴ Insidious, progressive loss of weight can be unnerving to caregivers and physicians, and sometimes leads to inappropriate work-up of what may be intrinsic to the pathophysiology of the disease. Contributing factors can include a low caloric intake, an

abnormally high expenditure of energy, or both. It has been suggested that AD may be associated with dysfunction in body weight regulation or a hypermetabolic state, although there are few data to this effect.⁵

Risk Factors

Several age-related factors place older adults at risk for malnutrition (Table 1).

Ageing. Even in the absence of cognitive dysfunction, older people experience decreased taste sensation to salty and sweet foods and an increase in threshold for the sense of smell. Impaired vision can interfere with the preparation and enjoyment of food. Poor dentition or ill-fitting dentures can influence the mechanics of eating. Chronic illness and depression can interfere with appetite and desire to eat. Medications can interfere with absorption of nutrients, and nausea with decreased appetite is a common drug-related side effect.

Dementia. With the development of dementia, the ambient risk for weight loss is compounded.⁶ Impaired ability to plan and prepare meals is a relevant factor, as is simply forgetting to eat. Food intake patterns also may be

altered. Nursing-home residents with AD and behavioral difficulties tend to have reduced meal-time food intakes over the course of the day.⁷ Patients with more advanced dementia also may experience shifts in their circadian eating patterns, such that the greatest proportion of daily energy is consumed at breakfast.⁷

Interaction with caregivers. It is important to realize, however, that weight loss also is routinely seen when a caregiver is available to help with meal preparation, and in institutionalized patients with AD. The nature of patient interaction with caregivers also appears to be important, both in the community⁸ and in the nursing home.⁹ The proportion of food consumed by nursing-home residents may be influenced by the quality of the interaction between the resident with AD and the person assigned to assist them with feeding.⁹

Dysphagia. Swallowing difficulties can contribute to decreased food intake in some people with dementia. This is commonly seen in vascular dementia or dementias associated with parkinsonism, in which pseudobulbar palsy can occur. (Recall that, in pseudobulbar palsy, there are swallowing

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difficulties which are subcortically mediated in the absence of demonstrable brainstem dysfunction—hence, “pseudobulbar”). Pseudobulbar dysphagia also can be a feature of AD—especially in the later stages¹⁰ and in association with other commonly seen signs and symptoms of autonomic disturbance¹¹—and may prompt a change in dietary consistency. Moreover, transient swallowing difficulties can be an “atypical” disease presentation in older adults.

The Search for Answers

Reports that weight loss often precedes the onset of AD by many years^{1,2} have prompted researchers to investigate alternate explanations. It has been suggested that an inappropriately high level of energy expenditure or a hypermetabolic state may contribute to unexplained weight loss in AD, however there is little empirical support for hypermetabolism as a significant contributor in most cases.^{12,13} Although there are individual cases where abnormally high levels of physical activity (e.g., pacing or ceaseless wandering) can result in excess energy expenditure and weight loss, the compromised mobility seen in advanced dementia leads to weight loss more commonly as a result of decreased muscle mass.¹⁴

Several other “biological disturbances” which accompany AD also have been considered as potentially contributing factors for weight loss.

Temporal lobe atrophy. Mention has been made of the considerable atrophy of the mesial temporal cortex in AD, but its relationship with weight loss remains unproven.

Leptin. Leptin is a peptide hormone that acts on the hypothalamus to regulate satiety and energy expenditure. The afferent limb of

Table 1

Factors that Predispose to Weight Loss in Older Adults

- Decreased taste sensation
- Decreased sense of smell
- Poor dentition/ill-fitting dentures
- Impaired vision
- Medications (e.g., psychotropic agents, digitalis, nonsteroidal anti-inflammatory drugs [NSAIDs], narcotics, theophylline)
- Depression
- Chronic illness
- Social isolation
- Dementia

the leptin feedback loop seems to be intact in underweight AD patients, leaving the possibility of hypothalamic dysfunction.¹⁵ Reduced intake of food may cause a decrease in the dynorphin-mediated feeding drive and an increase in the satiation effect of cholecystokinin, which may result in a “vicious cycle,” as malnutrition can cause increases in circulating cholecystokinin levels and further reduction of appetite.¹⁶

Apolipoprotein E-4. In women, otherwise unexplained weight loss has been associated with the apolipoprotein E-4 gene.¹⁷

Depression. Depression has been investigated as a function of weight loss in AD, but no persuasive relationship has been established.¹⁸

Inflammatory cytokines. It is both confusing and potentially enlightening that weight loss often occurs in AD despite adequate nutrient intake. This anomaly also occurs in cancer, raising the possibility of a common biochemical pathway of weight loss in malignancy and AD.¹⁹ Various inflammatory cytokines secreted by neoplasms, including tumor necrosis factor-alpha, interleukin-1 and interleukin-6, have been implicated in this process. Interleukin-6 has been found to be high in the brains of AD patients, suggesting a potential common mechanism.²⁰

Whatever the mechanism, it is instructive that, regardless of the patient’s nutrient intake, there is a shift towards catabolism, muscle wasting, weakness, and weight loss.²¹ This perhaps leads us to question the benefits to survival or quality of life from artificial feeding (enteral or parenteral nutrition) in advanced cancer or AD patients.²²⁻²⁴ That being said, an education program aimed at caregivers of AD patients without dysphagia found that fewer intervention patients experienced significant weight loss.²⁵

Interventions

Ironically, the two most commonly cited reasons for initiating tube feeding in advanced dementia—the prolongation of life and prevention of aspiration—are not supported by the evidence,^{24, 26} and this raises questions about the process by which decisions for tube feeding are made. A survey of nursing homes in Ottawa found that most tube-fed patients had not given advance directives and that the decisions in most cases were made by substitute decision-makers.²⁸ However, most of these substitute decision-makers spent less than 15 minutes discussing the decision with a physician and less than half felt that they understood the risks.^{26,27} Furthermore, most substitute decision-makers did not

feel the tube feeds improved the demented person's quality of life, and most said they would not choose to be tube-fed if they were in the same situation.^{26,27} Problems with substitute decision-making for enteral feeding are prevalent in both Canada and the United States,²⁶ although the indications for tube feeding are strikingly different. In Ottawa, long-term tube feeding was most often initiated following an acute neurological event, but rarely in dementia, whereas in Boston the reason for tube feeding was dementia in 60% of cases.²⁶

Other less invasive interventions may be beneficial. Offering meals at regular times of day and in a calm and consistent environment may be more acceptable to

the person with AD. There is some evidence that AD patients who consume most of their calories at breakfast are more prone to behavioral problems than those who do not, although this is felt to reflect changes in circadian rhythm, and not otherwise be the cause of the problem.⁷ Serving food that the patient likes and is easy to eat (e.g., finger foods, soups in a mug) and allowing sufficient time to eat are practical, low-cost interventions. Allowing snacks between meals and offering fluids regularly may help avoid dehydration. Individualizing the approach to feeding patients can be valuable. Recognizing that weight loss usually accompanies the progression of AD may help avoid inappropriate work-up, allay tensions around

mealtime and aid discussions about palliative care.

Physician's Role as Counselor

Families often wish to know whether patients with advanced dementia who do not eat are depressed or hungry. Without knowing exactly the "inner thoughts" of individual patients, clinicians can have an important counseling role in pointing out the separability of depression from dementia, and the usual absence of patient behavior indicating a desire to eat. Such discussions often work best if initiated by the clinician, rather than by the patient's family. Taking such initiative reassures families about both the thoughtfulness and competence of those caring for their loved one with dementia.

References:

1. Barrett-Connor E, Edelstein SL, Corey-Bloom J, et al. Weight loss precedes dementia in community-dwelling older adults. *J Am Geriatr Soc* 1996; 44:1147-52.
2. Barrett-Connor E, Edelstein S, Corey-Bloom J, et al. Weight loss precedes dementia in community-dwelling older adults. *J Nutr Health Aging* 1998; 2(2):113-114.
3. White H, Pieper C, Schmader K, et al. Weight change in Alzheimer's disease. *J Am Geriatr Soc* 1996; 44:265-72.
4. White H, Pieper C, Schmader K. The association of weight change in Alzheimer's disease with severity of disease and mortality: a longitudinal analysis. *J Am Geriatr Soc* 1998; 46:1223-27.
5. Rivière S, Gillette-Guyonnet S, Nourhashemi F, et al. Nutrition and Alzheimer's disease. *Nutrition Reviews* 1999; 57:363-7.
6. Shatenstein B, Kergoat MJ, Nadon S. Anthropometric changes over 5 years in elderly Canadians by age, gender, and cognitive status. *J Gerontol A Biol Sci Med Sci* 2001; 56(8):M483-8.
7. Young KW, Greenwood CE. Shift in diurnal feeding patterns in nursing home residents with Alzheimer's disease. *J Gerontol A Biol Sci Med Sci* 2001; 56(11):M700-6.
8. Gillette-Guyonnet S, Nourhashemi F, Andrieu S, et al. Weight loss in Alzheimer disease. *Am J Clin Nutr* 2000; 71(2):637S-42S.
9. Amella E. Factors influencing the proportion of food consumed by nursing home residents with dementia. *J Am Geriatr Soc* 1999; 47:879-85.
10. Chouinard J. Dysphagia in Alzheimer disease: a review. *J Nutr Health Aging* 2000; 4(4):214-7.
11. Siennicki-Lantz A, Lilja B, Elmstahl S. Orthostatic hypotension in Alzheimer's disease: result or cause of brain dysfunction? *Aging* 1999; 11(3):155-60.
12. Poehlman ET, Dvorak RV. Energy expenditure in Alzheimer's disease. *J Nutr Health Aging* 1998; 2(2):115-8.
13. Poehlman ET, Dvorak RV. Energy expenditure, energy intake, and weight loss in Alzheimer disease. *Am J Clin Nutr* 2000; 71(2):650S-5S.
14. Khodeir M, Conte EE, Morris JJ, et al. Effect of decreased mobility on body composition in patients with Alzheimer's disease. *J Nutr Health Aging* 2000; 4(1):19-24.
15. Power DA, Noel J, Collins R, et al. Circulating leptin levels and weight loss in Alzheimer's disease patients. *Dement Geriatr Cogn Disord* 2001; 12(2):167-70.
16. Barthelemy P, Bouisson M, Vellas B, et al. Postprandial cholecystokinin secretion in elderly with protein energy malnutrition. *J Am Geriatr Soc* 1992; 40:365-9.
17. Vanhanen M, Kivipelto M, Koivisto K, et al. APOE-epsilon 4 is associated with weight loss in women with AD: a population-based study. *Neurology* 2001; 56(5):655-9.
18. Purandare N, Burns A, Craig S, et al. Depressive symptoms in patients with Alzheimer's disease. *Int J Geriatric Psychiatry* 2001; 16(10):960-4.
19. Knittweis J. Weight loss in cancer and Alzheimer's disease is mediated by a similar pathway. *Med Hypotheses* 1999; 53(2):172-4.
20. Knittweis J. Weight loss precedes Alzheimer's disease symptoms: a case study. *J Am Geriatr Soc* 1998; 46(4):540-1.
21. Reynish W, Andrieu S, Nourhashemi F, et al. Nutritional factors and Alzheimer's disease. *J Gerontol A Biol Sci Med Sci* 2001; 56(11):M675-80.
22. Kim YI. To feed or not to feed: tube feeding in patients with advanced dementia. *Nutr Rev* 2001; 59:86-8.
23. Sanders DS, Carter MJ, D'Silva J, et al. Survival analysis in percutaneous endoscopic gastrostomy feeding: a worse outcome in patients with dementia. *Am J Gastroenterol* 2000; 95(6):1472-5.
24. Finucane TE, Christmas C, Travis K. Tube feeding in patients with advanced dementia: a review of the evidence. *JAMA* 1999; 282(14):1365-70.
25. Rivière S, Gillette-Guyonnet S, Voisin T, et al. A nutritional education program could prevent weight loss and slow cognitive decline in Alzheimer's disease. *J Nutr Health Aging* 2001; 5(4):295-9.
26. Mitchell SL, Kiely DK, Lipsitz LA. The risk factors and impact on survival of feeding-tube placement in nursing-home residents with severe cognitive impairment. *Arch Intern Med* 1997; 157(3):327-32.
27. Mitchell SL, Berkowitz RE, Lawson FM, et al. A cross-national survey of tube-feeding decisions in cognitively impaired older persons. *J Am Geriatr Soc* 2000; 48(4):391-7.
28. Mitchell SL, Lawson FM. Decision-making for long-term tube feeding in cognitively impaired elderly people. *CMAJ* 1999; 160(12):1705-9.