



Supplemental parenteral nutrition: decisions based on weak evidence



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Nutrition is essential for the physical and psychological well-being and for treatment tolerance in patients with cancer. Several biological systems are cooperating to provide our bodies with adequate nutrients and energy, the urge to seek food and eat, the oro-pharyngo-gastro-intestinal system to assimilate ingredients from meals and the metabolic system to guide and distribute the flow of nutrients among organs. If any of these systems fails to work normally, inadequate food intake may lead to deleterious consequences for quality of life and impact clinical outcome.

Therefore, international nutrition guidelines for patients with cancer recommend ensuring adequate intake of nutrients and energy by offering dietary counselling and if this proves inadequate, artificial nutrition (AN): primarily tube feeding, and if this proves inadequate, intravenous nutrition.¹ However, it needs to be considered that when deciding to use AN the evidence base differs depending on whether impaired food intake is caused by either anorexia in the context of activated systemic inflammation or by gastrointestinal defects in the setting of a more normal metabolism.

The desire to eat may be suppressed in an anorectic patient by psychological distress² or by metabolic derangements, which is most prominently related to disease-associated systemic inflammation.³ If metabolism is normal, either in a distressed anorectic person or in a patient with severely reduced food intake due to malfunction of the oro-pharyngo-gastro-intestinal system (eg, nausea, vomiting, stenosis, motility disorders, malabsorption), then AN is a viable option to substitute for oral foods, to circumvent the deficit and to supply the body with adequate amounts of nutrients.^{4,5}

In subjects with activated systemic inflammation, as is the case in many patients with advanced cancer, anorexia and gastrointestinal problems are usually accompanied by prevailing catabolism, including

compromised immunocompetence as well as accelerated protein breakdown, anabolic resistance and a sustained loss of muscle mass. There are no randomised trials in these settings demonstrating a benefit of AN over normal food or just fluids.⁶

In this issue a ‘targeted’ literature review on this topic highlights the present dismal situation. There is a small evidence base linking nutritional deficits in cancer patients with reductions in overall survival; however, there are no reliable data to judge the benefit of providing AN in patients with advanced cancer.

Scanning nearly 30 years of research the authors found no clinical trials evaluating clinical or economical effects of optional supplemental parenteral nutrition (SPN)—which is offered in addition to normal food—in cancer patients at risk of or presenting with malnutrition. Four one-armed observational trials reported on the evolution of nutritional markers during SPN; one randomised controlled trial documented an increase in fat-free mass associated with SPN but failed to differentiate whether this was due to an increase in cell mass or water.

Webb *et al*⁷ proceed to more indirect arguments linking effects of parenteral nutrition on several biomarkers obtained in a small set of trials with associations between these biomarkers and clinical outcome as reported in another set of trials⁷. Combining these observations, they calculate a small hypothetical prolongation of life resulting from SPN. This is hypothesis-generating at its most basic level and cannot guide clinical decisions today.

The authors then take another step into the blue air by calculating the incremental cost-effectiveness of SPN, using the virtual survival benefit and the cost of AN as well as of nursing and home delivery. Dignified by a currency symbol, this is suggesting serious and well-validated numbers, but it is in fact walking blindly on the edge of a cliff.

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What can we learn from this? Nutrition is essential but severely understudied in patients with advanced cancer. When faced with decision-making, there is hardly any solid evidence to step on, rather we have to swim in the swirling waters of uncertainty. What we and our patients desperately need are high-quality trials in homogeneous populations of adequate size, stratified for causes leading to reduced food intake, providing transparent feeding procedures for adequate time periods and, last but not least, including plausible and clinically relevant comparator arms.

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