

Nutritional therapy for cancer patients

Leczenie żywieniowe pacjentów onkologicznych

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Abstract

Only in 2016–2017, 954 works on cachexia, including 370 review articles and comments, 254 case studies and other non-randomized studies, 246 basic studies, and 26 randomized trials were published. There were 147 publications with 10 or more citations and 25% of them came from 5 journals (there were 478 journals interested in the cachexia problem in the analyzed period worldwide). The progress of cachexia research towards randomized trials and the growing number of publications in general foster the search for new therapies. The contents of Polish Medical Bibliography prove a great interest in the nutritional treatment of oncological patients among dietitians and slightly less interest among oncologists. Pharmacists are also interested in advising in multi-specialized cancer therapy. This indicates the awareness of the significance of the problem among representatives of many different disciplines. Step by step, the problem of oncological patients treatment ceases to be an exclusive concern for oncologists and this is good news given growing challenges of systemic treatment. On the other hand, it should be mentioned that nutritional treatment serves only an auxiliary function in comprehensive cancer therapy. An aim of this article is to recollect basic standards in the nutritional treatment of oncological patients, while new methods of therapy are awaited.

Key words: oncology, nutritional therapy, cancer patient, clinical nutrition

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Streszczenie

Tylko w latach 2016–2017 opublikowano łącznie 954 prace o kacheksji, w tym 370 artykułów przeglądowych i komentarzy, 254 studiów przypadku i innych badań nierandomizowanych, 246 badań podstawowych i 26 badań randomizowanych. Publikacji na ten temat o liczbie cytowań 10 lub więcej było 147, z czego 25% pochodziło z 5 czasopism (w analizowanym okresie problem kacheksji zainteresował 478 redakcji na świecie). Postęp badań nad tym zagadnieniem w kierunku prób randomizowanych i zwiększająca się liczba publikacji ogółem sprzyjają poszukiwaniu nowych metod terapii. Polska Bibliografia Lekarska dowodzi dużego zainteresowania leczeniem żywieniowym pacjentów chorych na nowotwory wśród dietetyków i nieco tylko mniejszego u onkologów. Także farmaceuci są zainteresowani doradzaniem w wielospecjalistycznej terapii nowotworów. Wskazuje to na duże znaczenie problemu uświadamiane przez przedstawicieli wielu różnych dyscyplin. Coraz częściej problem pacjentami chorymi na nowotwory zajmują się inni specjaliści niż onkolodzy, co powinno cieszyć wobec dużych wyzwań leczenia systemowego. Z drugiej strony należy pamiętać, że leczenie żywieniowe spełnia tylko pomocniczą funkcję w kompleksowej terapii nowotworów. Celem artykułu jest przypomnienie podstawowych standardów leczenia żywieniowego pacjentów chorych na nowotwory w oczekiwaniu na nowe metody terapii.

Słowa kluczowe: onkologia, leczenie żywieniowe, pacjent onkologiczny, dietetyka kliniczna

Taking into account research reports regarding the use of new preparations, it seems to be necessary to remind about the current knowledge regarding nutritional proceeding with an oncological patient.^{1,2} The nutritionist faces a challenge in the form of controlling the patient, who often suffers from cognitive disorders pertaining to chemotherapy or does not follow therapeutic recommendations.^{3–6} Such counseling is often at odds with the standard of multi-specialized care over the patient.⁶ In addition, its difficulty increases due to concomitance with systematic treatment.^{7,8}

Due to the justifiability and effectiveness of nutritional treatment of oncological patients, they were given the A category in the evidence hierarchy according to evidence-based medicine.⁹ In this category of patients, the problem of malnutrition or wasting occurs with the frequency of 30–85%, thus being the direct cause of death for 5–20% of patients (broader scopes of malnutrition indicators and cachexia are being assumed lately: 3–83% and 28–57%, respectively).^{10–16} Malnutrition intensifies in the terminal stage of the disease. Cachexia-anorexia syndrome depends on the disruption of oral feeding, increase of the loss of nutrients, intensification of Cori cycle, more intense utilization of proteins and carbohydrate and fat metabolism, increase of inflammatory reactions due to pro-inflammatory cytokines, increased catabolism due to circling factors, and greater energy demand caused by huge energy expenditure (a side effect of anti-cancer therapy).^{9,15,17} There is lack of credible research indicating the dependency between nutritional therapy and the risk of accelerating the cancer process; however, it has been determined that starvation diet makes the patients condition worse.^{13–15}

It is advisable to include nutritional counseling at every stage of oncological treatment, beginning at secondary prevention and the moment of diagnosis, continuing throughout the period of active treatment (applied therapy notwithstanding) and recovery, and ending at palliative care.^{18–21} It also constitutes the safest, cheapest and simplest way of maintaining and even improving

the state of many patients.^{9,15} It is recommended for the nutritionist's care to be extended not only to cured patients or during periods of longer remissions, but also to the ones afflicted with malnutrition resulting from a significant disruption of the anatomy and physiology of the gastrointestinal tract (especially the ones afflicted with head and neck tumors, as well as the upper gastrointestinal tract tumors). The significant importance of obesity treatment for the secondary prevention in the case of women who had been diagnosed with estrogen-dependent, postmenopausal breast cancer, was demonstrated.¹⁵ The obligatory elements of nutritional counsel are: medical documentation analysis, detailed dietary history, dietary state assessment, calculation of demand for particular macro- and micronutrients, selection of nutritional recommendations (diet based upon basic products, food fortification, oral industrial diets), recommendations understandable by the patient, and entry into medical documentation.¹⁵

Many non-specific research tools are applied in malnutrition risk diagnostic, i.e., Subjective Global Assessment (SGA), Nutritional Risk Screening 2002 (NRS 2002), preferred by the European Society for Clinical Nutrition and Metabolism (ESPEN), as well as Malnutrition Universal Screening Tool (MUST) including the variant for the elderly (Mini Nutritional Assessment (MNA)).^{9,10,12,17} Test tools supplement the physical examination techniques (interview), but also anthropometric measurements and biochemical research.^{15,16} Source literature recommends triangulation of the aforementioned methods.⁹

Selection of treatment depends on the patient's condition, degree and type of malnutrition, and planned period and time of feeding (pre-surgical and post-surgical).⁹ Enteral nutrition is the preferred method which covers: oral food intake (including fortification), application of oral industrial diets (sip feeding), gastric nutrition (gastric tube or gastrostomy tube), and enteral nutrition (gastric tube or J-tube).^{9,16} Patients who cannot be provided with at least 60% of nutritional demand have their enteral diet supplemented with parenteral diet. Patients who cannot

be fed orally are fed exclusively enterally. In turn, an integral element of enteral nutrition is the satisfaction of the organism's demand for all amino acids, lipid emulsions, electrolytes (Na, K, Ca, Mg, Cl, P), trace elements, vitamins (retinol, cholecalciferol, tocopherol, vitamin K, thiamine, riboflavin, pyridoxine, vitamin B₁₂, pantothenic, folic and ascorbic acid, niacin), water, and glucose required in the diet.⁹ Due to the above, it has been assumed to make a distinction between complete and incomplete diet, whereas only the first one provides all of the required proteins, electrolytes, vitamins, trace elements and water, and satisfies energy demand in full. When analyzing the detailed application nutrients of the aforementioned groups in the feeding of oncological patients, the following are pointed out: the effect of glutamine supporting correct functioning of immune cells and intestinal epithelium, the role of arginine in wound healing, protein biosynthesis and many non-protein based metabolic cycles (shortages of arginine are determined following great traumas and in cachexia), and the role nucleotide acids in intestinal villi regeneration and optimization of the immune system at increased demand in states of intense metabolism.⁹ When settling the application of polyunsaturated fatty acids in the oncological patients' diet, it should be noted that they constitute elements which are completely exogenous, i.e., their intake is absolutely necessary, all the more that certain tests have confirmed their therapeutic effect in cancer treatment,⁹ with the difference that whereas n-3 acids show anti-inflammatory action, n-6 acids do the opposite.⁹ Diet should provide all necessary nutrients in quantity adequate to daily need, as well as satisfy energy demand in full. However, it is recommended to increase the proportion of proteins and energy value in food for patients afflicted with cachexia.⁹

Recommendations for nutritional treatment for patients suffering from cancer are the same as for the other patient groups: lack of possibility of oral food intake for more than 7 days, actual malnutrition or threat thereof, and lack of satisfaction of 60% of energy need for more than 10 days, B or C degree in the SGA scale, as well as 3 points or more in NRS 2002.^{9,10} Among the patients directed to nutritional treatment, those whose body mass index (BMI) is ≤ 18.5 kg/m² or the albumin concentration in serum is < 30 g/L or who have lost at least 10–15% of body mass during the last 6 months should receive help as soon as possible (however, not earlier than following the regulation of the metabolic state).¹² The remaining border values are weekly and monthly body mass loss – not greater than, respectively, 2% and 5% of the original mass, < 3.5 g/dL of albumin, < 16 mg/dL of prealbumin, and < 200 mg/dL of transferrin concentration, with a preference for transferrin and prealbumin in the assessment of quickly emerging consequences of malnutrition.¹⁵ Incorrect total lymphocyte count (CLL), abnormalities of skin response to antigens and gradual lymphopenia are also biochemical indicators of malnutrition. Other anthropometric

indicators, besides the ones connected with weight and height, are: skin and fat pad measurement – the volume of subcutaneous fat tissue, arm circumference, arm muscle measurement, and arm muscle surface indicators – muscle tissue reserves showing the volume of protein.¹⁵

Fortification is the increase of a diet's nutritional value by adding natural products featuring great calorie density (e.g., butter, cream, chocolate, honey, yolk (vitellus), plant oils, coconut milk, dense groats, ground nuts, meat) or with the help of mono- or multi-compound industrial preparations supplementing the diet.⁹ Mono-compound preparations contain proteins, carbohydrates or fats, while multi-compound ones contain their combinations, often with the addition of vitamins and minerals.⁹ Fortification of a diet often requires a variation of its texture with simultaneous variation of the volume and frequency of meals depending on the limited appetite and ailment of the patient. Improperly fortified diet may constitute deficient food, which is why the help of qualified personnel is necessary.⁹

Oral industrial diets are for patients with malnutrition or ones who are in danger of malnutrition. In accordance with Commission Directive 1999/21/EC of 25 March 1999 of the European Union, they must be supervised by a qualified personnel.⁹ Preparations can be both complete as well as incomplete, which means that only the former contain all of the required macro- and micronutrients of the diet. Standard preparations reflect the composition and proportions of a normal oral diet, whereas special preparations fulfil non-specific nutritional recommendations relevant for disease entities.⁹ The advantages of oral industrial diets are: concentration of calories and nutritional compounds in small volume, ease of use (preparations can be mixed with natural products, they can be also cooled or heated up a little), the possibility of adjusting the composition to the organism's requirements in a given disease (e.g., low-protein preparations for patients with kidney failure in pre-dialysis stage), lack of potentially harmful compounds (lactose, gluten, purine, or cholesterol), as well as possibility of applying preparations featuring fiber or devoid of fiber, and aseptic packaging (UHT sterilized), thus with not bacterial contamination.⁹ However, the application of oral diets is burdened with the following requirements: the patient does not vomit and has the swallowing ability intact (dysphagia requires food featuring special texture; otherwise, oral diet is completely excluded), and obstruction of gastrointestinal tract, heavy inflammation or ileus, as well as gastrointestinal fistula are excluded.⁹ Due to caloric value, oral preparations are divided into: hypo- (diet of 0.5–0.9 kcal/mL), iso- (diet of 1.0–1.2 kcal/mL) and hypercaloric (diet of 1.3–2.4 kcal/mL).¹⁰ The serving of hypocaloric preparations in carbohydrate-electrolyte form is limited to being performed prior to surgeries. Isocaloric multi-compound preparations have a wider range of applications: They are recommended for persons afflicted with diabetes,

cachexia or ones who were starved for a long period of time. The task of the preparation in the case of the last group is to prevent the refeeding syndrome during the re-adaptation period to full protein-energy requirement. Isocaloric diets are well-tolerated especially by patients who had gastrectomy, pancreatic resection and ileostomy performed on them. Following the period of isocaloric preparation application, it is possible to proceed to hypercaloric preparations. They are applicable for patients with malnutrition or those with no appetite – however, at the cost of high solution osmolality which provokes diarrhea, flatulence and nausea.^{9,12}

Enteral nutrition with the use of gastric tube or fistula is recommended for patients who cannot be fed orally, who are dealing with swallowing disorders caused by a tumor, mucosal reaction and/or complications following radio or chemotherapy of neck, as well as during the early post-surgery period and during the treatment of complications of the upper gastrointestinal tract.^{9,12} On the other hand, this type of nutrition is not recommended for patients diagnosed with: ileus or intestinal ischemia, malabsorption, lingering diarrhea, and emesis, or in heavy shock.¹² Selection of access mode to the gastrointestinal tract depends on the type and degree of cancer progress, as well as the projected feeding period. Nasogastric or nasoenteral tubes are used in patients whose projected feeding time is shorter than 30 days.⁹ Due to the small diameter of the tube, its placement does not block the strictures causing the dysphagia, provided that the procedure is performed under endoscopic control. Gravitationally distributed food or one distributed with the use of peristaltic pumps contains completely liquid very low-calorie diets (VLCDs) specially prepared for enteral nutrition.¹⁶ The infusion rate is increased gradually, starting from 10 mL/h, but not too fast, in order to achieve optimal intake only following 5–7 days. Only in gastric tubes it is possible to provide food in boli featuring a volume of 200–300 mL.⁹ Admittedly, the small diameter of the tube makes food intake possible for patients with stricture, but it may be blocked by the digesta or may be the cause of an accidental removal by the patient. Medications taken by the patient also have to be prepared in the form of a liquid or a special solution.⁹

Gastrostomy is a gastric access for a time period >30 days, placed using classic surgical method, laparoscope or endoscope. Its small degree of invasiveness makes it the procedure of choice. However, there are the following contraindications: serious coagulation abnormalities, intraperitoneal carcinomatosis, peritonitis and intensified ascites, or interposition of abdominal cavity organs.⁹ The most frequent complications are: wound and gastrostomy area infections, catheter blockage, leaking from and lack of tightness around gastrostomy area, gastrostomy falling out, and development of PEG (percutaneous endoscopic gastrostomy) mushroom (buried bumper syndrome).⁹ Feeding takes place 5–6 times per day with boli of

200–300 mL or microboli of 50–100 mL, or with the use of constant infusion at the rate of 20–30 mL/h.¹⁴ Kitchen food is admittedly allowed for gastrostomy; however, it is harder to apply than industrial diet. Its nutritional value cannot be determined precisely, which increases the risk of error.⁹

Microjejunostomy is the method of choice if gastric access is impossible (or not recommended) or when the stomach is planned to be used in restoring the continuity of the gastrointestinal tract in esophagus surgery and esophagus-stomach connection. It is placed using the classic method, or with the use of laparoscope or sets for needle catheter jejunostomy.⁹ Microjejunostomy imposes limitations within the scope of the type of food. It can be only an industrial diet adjusted in terms of composition and osmolality to the physiology of the small intestine. Such diet is suitable for intake in gravity drop infusions or with the use of peristaltic pumps at a rate as in gastric infusion (initial speed 10 mL/h, increased up to the optimal one during a period of 5–7 days). As opposed to the gastric access methods, there is no possibility of applying boli. This is due to the fact that the usage of boli, as well as too fast infusion rate, leads to diarrhea, abdominal pain and flatulence.⁹

Lack of the possibility of providing food via gastrointestinal tract forces one to total parenteral nutrition (TPN).¹⁴ In the event of the limited possibility of food intake via this way, partial parenteral nutrition is applied.⁹ Its task is only to supplement the diet, as opposed to total parenteral nutrition, in which the entirety of nutritional substances has to be provided in parenteral manner. The “all-in-one” method is used, which consists in mixing all of the food compounds in only 1 container. This increases food tolerance and, besides that, reduces the number of infections and lowers the costs.⁹ Parenteral nutrition takes place with the use of a central catheter placed in the connection of the upper main vein and the right atrium of the heart – parenteral nutrition via peripheral way (most often it is a forearm vein), arteriovenous fistula (used also for hemodialysis or placed specially for this purpose – only in patients with the excluded possibility of a central venous catheter), central vascular access port underneath the skin of the chest cavity (totally implanted device (TIP)).^{14,22,23} Access ports to peripheral veins limit the feeding period to 7 days. It is applied, above all else, as a method of necessity when central access is impossible.⁹ In terms of complications, metabolic disorders in the form of glycemia or hydro-electrolyte disorders predominate. Refeeding syndrome is also a disorder of this type.¹² Infections in venous access locations are rarer than metabolic disorders. Technical problems connected with the placement and later maintenance of access occur sporadically.⁹ Non-specific elements in nutritional treatment are the immunomodulating factors contained within the diet. Their purpose is to reinforce immunological barriers, to fight the inflammatory state and to weaken the systematic

cytotoxic reaction.⁹ Such substances are, i.a.: glutamine and arginine amino acids, nucleotide acids, and n-3 fatty acids. It should also be added that the therapeutic effect was not indicated in huge, randomized populations.^{9,15} More frequent need of a lactose-free diet is characteristic for radiotherapy patients. However, it is not a standard diet, but one forced by the damage done to the functions of the intestinal epithelium which, besides chemotherapy, are encountered in treatment with cytotoxics.^{9,24} In terms of gluten-free diet, in oncology it becomes necessary only in some cases of heavy radiation enteritis or heavy chemotherapy enteritis (omitting the coeliac disease concurrently taking place).⁹ Supplementation with vitamins or minerals is not a routine procedure in malignant tumor therapy, which is why it is implemented only in the event of documented shortage of a compound or depending on the patient's state, which must lead to a shortage.¹ Radiation enteritis mentioned when discussing gluten-free diet is a clinical situation requiring to be discussed in detail. It occurs as a result of radiotherapy of the abdominal cavity or pelvis minor with subsequent gastrointestinal complications. It has been shown that the increased frequency of radiotherapy in multidisciplinary cancer therapy translates into a higher number of such complications.⁹ However, it is not possible to accurately estimate their number due to hardly noticeable changes in lighter cases. The difficulty of estimation is also exacerbated by the fact that some of the changes are revealed even many years after the treatment is completed. The (very imprecise) range of 2–30% is therefore taken as an approximation.⁹ Two variants of radiation enteropathy are encountered: topical with recommended pharmacological treatment and fluid therapy or parenteral nutrition, and – besides – surgical intervention as a method of necessity; diffuse with parenteral nutrition as an initial option, followed by home parenteral nutrition and finally, oral.⁹ Surgical intervention is the last resort also in diffuse enteropathy. Patients with radiation-induced chronic disorders constitute a separate group. They must undergo many ad hoc surgeries to remove the causes of intestinal obstruction. However, such patients often receive continuous parenteral nutrition (without the necessity of surgery), including at home.⁹

The most characteristic problem in the nutrition of oncological patients is diet during chemotherapy. A significant proportion of people – 79% – experience the effects of chemotherapy on their diet at least once a month, 72% as many as 6 chemotherapy-related factors per month, and 46% – 12 factors.¹⁰ Side effects compounded by progressive cancer significantly increase the risk of nutritional deficiencies.¹ Weight loss occurs even in 91.8% of patients during or after chemotherapy, and weight loss increases with the cycle also in patients diagnosed with non-gastrointestinal cancers – the intrinsic effect of chemotherapy.¹⁰ Patients are advised to eat small but frequent meals, rather cold, of weak aroma and, above all, easily digestible. These are: soups and creams, fruit

and fruit-and-milk shakes, vegetable and fruit mousses, water-diluted juices, jellies, pudding, ice cream, sorbets, omelets, pancakes, cottage cheese, and small groats.⁹ Diarrhea requires a BRAT diet (acronym derived from its ingredients: B – bananas, R – rice, A – apples, T – toasts) with oral water and electrolyte refill. In the case of constipation, it is crucial to determine the cause. In some types of constipation, e.g., due to the 5-HT₃ receptor inhibitor, a special diet is unnecessary. Constipation after opioids requires both pharmacological treatment and dietary support.⁹

The greatest successes of nutritional treatment in oncology are visible in pre- and postoperative periods. Research has shown a positive correlation between preoperative patient dietary support and treatment outcomes in terms of both immediate and distant effects, as well as between dietary support and improving quality of life.⁹ Thus, the principle is to increase meals for preoperative patients with profound malnutrition.¹⁴ The lack of nutritional improvement in patients is also an indicator of progress in the cancer process and argues for the ineffectiveness of radical therapeutic measures.⁹ The benefits of nutritional treatment for patients who are moderately undernourished or only at risk of malnutrition are usually lower, but such patients also achieve general improvement and a reduction in the risk of postoperative complications.⁹ The diet of preoperative patients is supplemented with immunomodulating preparations. However, there is a lack of clear evidence of their efficacy.⁹ According to the Enhanced Recovery After Surgery (ERAS) recommendations, 400 mL of carbohydrate fluids are administered orally up to 2 h before surgery. This prevents postoperative insulin resistance, hyperglycemia, excessive protein and body weight loss, as well as strengthens the condition of muscles, reduces postoperative anxiety and reduces the risk of nausea and vomiting. Carbohydrate fluid can be replaced by 20% glucose administered intravenously at a dose of 5 mg/kg body weight.⁹

Also according to ERAS, postoperative patients with no signs of malnutrition are provided with an oral diet of at least 60% of their energy requirements as soon as possible.⁹ In patients with no possibility of oral food supply, a tube or nutritional intestinal fistula is used instead of central vascular access due to the higher risk of postoperative complications. Industrial preparations are used. The nutritional treatment in the presence of postoperative complications is carried out according to general rules except for gastrointestinal fistulas. Due to the risk of serious health consequences and even death, treatment is carried out in the surgical ward.⁹

Lower gastrointestinal surgery usually does not require a special postoperative diet. This is different for esophageal, stomach or pancreatic surgery, where dietary advice is almost always necessary.¹ In addition, patients after extensive resections are exposed to short bowel syndrome. For an oral diet, the length of the small intestine sec-

tion that must be preserved is 100 cm, and 65 cm in the case of jejunocolic anastomosis. Shorter stretches eliminate oral diet.⁹ Symptoms of short bowel syndrome include diarrhea, fatty stools, weight loss, dehydration, and malnutrition due to insufficient absorption of macronutrients, vitamins, fluids, electrolytes, and trace elements, followed by hypovolemia, hypoalbuminemia and metabolic acidosis.⁹ Possible complications include: excessive hydrochloric acid, D-lactic acidosis, kidney stone disease, oxalate nephropathy, cholelithiasis, and liver dysfunction.⁹ Treatment consists of 3 stages: immediate postoperative period, intestinal adaptation period and long-term treatment. Immediately following the operation, fluid and electrolyte losses are replenished, hydrochloric acid is reduced, secretory and motor activity of the digestive tract is inhibited, and parenteral nutrition is implemented. Large losses should be monitored and then compensated for up to daily diuresis levels above 1,000 mL. Parenteral nutrition should take place as early as possible, in order to counteract or prevent malnutrition. Enteral nutrition should be incorporated slowly, depending on the amount of stool excreted. However, in more severe cases, parenteral nutrition remains a necessity for the rest of one's life.⁹

Oncological patients with head or neck cancer constitute a special group in terms of nutrition. They are often characterized by malnutrition already at the beginning of oncological therapy. Malnutrition is determined in 80% of patients.¹⁷ This is due to the fact that head and neck cancers are second only to ovarian and uterine cancers in terms of frequency.¹⁰ Nutritional treatment is a part of integrated therapy, although it is not standalone, but serves as a therapeutic aid.⁹ According to ESPEN, there are no recommendations for mandatory inclusion of enteral nutrition in patients with neck or head cancer undergoing radio or chemotherapy, unless they have or are expected to have swallowing disorders. Therefore, standard recommendations are required.⁹ However, studies have shown that nutritional treatment has a beneficial effect on the improvement of general condition. Enteral nutrition, including oral preparations, with preferred methods of endoscopic gastrostomy and nutritional fistulas, is most commonly used only in cases of exclusion or restriction of the oral route.⁹

Conclusions

Malnutrition and its extreme form – cachexia – constitutes a common problem in oncological patients, especially in the terminal stage of the disease, and in certain types of cancer.

Although the effectiveness of nutritional treatment has been confirmed only for preoperative patients, it is a general standard, as starvation always worsens the patient's condition.

Currently available nutritional treatment (as part of a comprehensive cancer therapy) constitutes the simplest, safest and cheapest way to improve the comfort of the patient, especially when undergoing chemo- or radiotherapy.

There is a lack of evaluation studies of new therapy methods in large-scale randomized trials. This does not change the fact that numerous basic studies, case studies and other unrepresentative studies are sources of inspiring hypotheses.

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