To my fellow oncology dietitians,

As we approach the end of this decade, I wanted to express my deepest gratitude for each and every one of you and the hard, yet fulfilling, work that you do every day. During this time, the role of the oncology dietitian as a member of the patient care team has grown from one that was considered extraneous into one that is becoming essential for providing patients with the best possible care. Much of this change has been made possible not only by the research, networking, and advocacy of ON DPG members, but also as a result of oncology dietitians on the front lines. Each of you continues to show up on a daily and demonstrate the integral, non-negotiable role RDs play in the care of our patients. While we still have far to go in order to make the dream into an absolute reality, each day we get a little closer. Thank you for all that you do, and let’s make this next decade of oncology nutrition the most memorable one yet!

I loved being able to connect with so many of you in person at FNCE®! It is inspiring to meet so many like-minded RDs who deal with many of the same issues on a daily basis, no matter where in the country they are stationed. We had a blast at our member reception at MANNA, where we learned about how the organization serves cancer patients, not only through their meal delivery program, but also by offering nutrition counseling provided by a great team of RDs. During this time, we were also able to honor many of our award winners in person; I won’t list them all out here, but check out the list of award winners on our website to see the great work that they’ve been doing and the solid partnerships that the ON DPG has been forming on your behalf. Your Executive Committee has been brainstorming themes for next year’s FNCE®, and this year rocked the 80s theme (a la Rocky) at the membership booth. Finally, the ON DPG spotlight session, “Sarcopenia in Cancer,” provided great insight into the underdiagnosis of sarcopenia in cancer patients, as well as the power of good

(Continued on next page)
networking are endless and it is truly a valuable experience to meet the individuals whose names you see every day on the discussion forums — so get yourselves registered ASAP as we've sold out quickly in past years and are expected to again!

Finally, I know that the transition from the EML to the discussion forums was very sudden and without much forewarning. I wanted to thank everyone for their understanding and patience with the transition and hope that you will find a great benefit in the new formatting. Please don't hesitate to contact us with any questions or concerns.

Wishing you and your families a wonderful holiday season and a very happy start to 2020!

Warm regards,
Caitlin Benda, MBA, MS, RDN, CSO
Chair, ON-DPG

PS – Don’t forget to follow us on Facebook, Twitter, and LinkedIn as we continue to grow our social media presence!
Feeding with More Than Food: A Novel Multidisciplinary Approach to Combat Pediatric Malnutrition

By Christina Stella MS, RDN, CDN, CDE and Hannah Husby MS, RDN, CDN

Abstract
Pediatric cancer patients are a vulnerable population, often presenting at high nutritional risk. Therefore, the role of the registered dietitian nutritionist (RDN) in caring for the pediatric cancer patient is imperative. The RDN can positively impact clinical parameters such as growth, development, and laboratory values, but also meaningfully impact a patient’s quality of life, such as providing culturally appropriate meals or involving the patients in meal preparation. This article will address some pediatric malnutrition screening tools, the rates and impact of pediatric malnutrition, how to plan non-medical nutrition therapy activities oriented towards improving nutrition status and scope of practice for the RDN. This article will also address how interdisciplinary teams can positively impact the care of pediatric patients, as the theme “it takes a village” has resonated in many medical centers as one of the most important ways to disseminate good patient care.

The role of the RDN in caring for the pediatric cancer patient is imperative. Whether it is the metabolic burden of a catabolic illness, deficiencies associated with nutrient needs and losses or side effects of anti-cancer treatments, or psycho-socio limitations, pediatric patients may encounter prolonged periods of inadequate oral intake and subsequently malnutrition (1). Some of the negative consequences of malnutrition include: longer lengths of stays, increased financial costs, decreased treatment responses, reduction in the quality of life, and lack of growth and/or development (1). Although rates of survivorship continue to improve, rates of malnutrition have not decreased at the same rate and continue to be reported in varying degrees. Malnutrition rates in the pediatric population may be as low as 6% or as high as 50% (1-3). In addition, certain types of cancer and the presence of metastatic disease predispose patients to greater risk of malnutrition. For example, Yoruk et al. evaluated the nutrition status of pediatric oncology patients at diagnosis and over a six-month period, and found 10.9% undernutrition and malnutrition in patients with hematologic malignancies. In patients with solid tumors, 16.7% patients were undernourished, and 22.2% had malnutrition. (4). Many studies have looked at the etiology of the variation in undernutrition and malnutrition. Variation in prevalence is thought to be due to: treatment with multiple therapies, combinations and intensities of the therapies, vastly different standards of living, and difference in criteria to diagnose malnutrition (5-7). A strong commitment to define and set parameters regarding undernutrition and malnutrition can potentially close the gap, and this work is ongoing at both the Academy of Nutrition and Dietetics (the Academy) and American Society of Parenteral and Enteral Nutrition (ASPEN).

The two most widely studied and subsequently utilized tools are Screening Tool Risk on Nutrition Status and Growth (STRONGkids), and Pediatric Yorkhill Malnutrition Score (PYMS). STRONGkids is a score-based screening tool where the following parameters are measured and assessed: fat losses, high risk disease, nutritional intake and losses, and weight loss and/or poor weight gain. Risk of malnutrition is associated with higher scores. Several researchers have investigated this tool’s success in identifying under- and malnutrition, (Continued on next page)
when administered by a non-nutrition professional, since that is a key feature of this tool. For example, STRONGkids recognized 84% of undernourished children when the tool was applied by nurses and 90% when the tool was applied by a pediatrician, indicating substantial agreement, kappa = 0.65 (15). In addition, a higher STRONGkids score also correlates with longer lengths of stay and need for nutrition interventions. Huysentruyt et al reported that higher STRONGkids scores significantly correlated with the need for nutritional intervention (OR, 18.93; 95% CI, 4.48-80.00; P < 0.01) (16).

PYMS is another validated screening tool that determines the risk score from an assessment of body mass index (BMI), weight loss, and dietary intake. Due to the inclusion of anthropometrics, PYMS may identify more malnourished children as demonstrated by Beser et al who explored the prevalence of malnutrition risk in hospitalized children by applying the STRONGkids and PYMS screening tools (17). PYMS captured a greater percentage of high-risk patients, and the authors felt the use of anthropometrics prevented some patients who were at nutrition risk from being overlooked (17). In a study evaluating nursing feedback on PYMS, 96% of the nurse respondents found the tool to be easy to use, and 85% reported it took less than 5 minutes to complete (18). The Subjective Global Nutrition Assessment has been found in many studies to be the gold standard of screening tools and various pediatric screening tools are compared to this standard, including the PYMS. Wonoputri et al compared the PYMS, STRONGkids, and Screening Tool for the Assessment of Malnutrition in Paediatrics (STAMP) against the Subjective Global Nutrition Assessment, which despite the lack of a universal screening tool is considered the gold standard. The PYMS had the smallest percentage of false-positive results, with 95.31% sensitivity, and 76.92% specificity (19).

Although anthropometrics proved to be essential assessment criteria, some studies have found conflicting information regarding use of anthropometric measurements alone to identify nutrition risk and subsequently malnutrition. BMI masked malnutrition associated with solid tumors (20), and researchers recommend that screenings involving BMI should be used in conjunction with other parameters or interpreted cautiously when using it as a sole indicator of malnutrition. Review of pediatric nutrition screening tools suggests quality care involves screening, and clinical measurements, like anthropometrics, should become part of the screening. However, because of differences in screening parameters, disease categories, and how personnel conduct screening, it is important to work towards identifying the type of screening tool that will accurately assess malnutrition early and lead to faster treatments and greater efficacy. Routine multidisciplinary screening is the first step in best nutritional care.

All members of the healthcare team should collaborate to ensure that screening for malnutrition becomes an integral part of routine pediatric care (21). At MSK, screening is multi-disciplinary and encourages various members of the medical team to be involved with the nutritional care of patients in accordance with recommendations from the Academy and ASPEN. All patients are screened upon admission by the registered nurse (RN) and patients that present with positive nutrition risk factors are referred to the RDN. A nursing referral is generated if a patient responds positively that they are experiencing
weight loss, newly diagnosed diabetes, appetite loss, difficulty swallowing, mucositis/stomatitis, vomiting, or diarrhea. Physicians and other members of the medical team also screen patients for nutrition risk and generate referrals to the RDN, which focus on nutrition education, tube feed initiation and management, and optimization of nutrition. MSK also uses secondary risk criteria that allows RDNs and other members of the clinical team to screen patients to ensure no patient is missed that would benefit from a nutrition-focused intervention. These risk criteria that were developed in coordination with the inpatient dietitian team and physician champions from each oncology service pertain to high risk medical diagnosis, treatments, admission location, and malnutrition itself (Table 1). The use of secondary risk criteria assumes more children at high nutritional risk will be identified because screening utilizes more than just anthropometrics and oral intake. Secondary risk criteria are important to include since some studies have identified deficits in the ability of just anthropometrics and intake to capture all high-risk children (20). Establishing additional criteria to identify nutrition risk can shorten the length of time it takes to initiate nutrition interventions and allows all members of the medical team to work together to ensure quality care of at-risk patients. Since the use of a pediatric screening tool is not universally defined, MSK combines aspects of various tools in an effort to capture the greatest number of patients at nutrition risk. These have also been identified as areas where Institutions can participate in research and/or quality improvement projects with the goal of using the screening tool that is not only valid but understands specific populations best in terms of nutrition risk.

The role of the RDN revolves around the identification of undernutrition, malnutrition, and providing interventions to improve or resolve nutritional concerns. Often, the RDN’s responsibilities in the management of pediatric cancer involves working with patients and families to provide nourishing meals. These meals need to not only meet the patient’s nutrient needs, but must also consider changing taste perceptions and symptoms and side effects of treatments that limit intake. At MSK, several initiatives take place with the goal of improving the patient experience and optimizing nutritional status. MSK utilizes a room service style meal delivery program, a growing trend in hospital food service. The MSK program allows patients to order meals and snacks according to their preferences anytime throughout the day. This has been shown to improve patient satisfaction and improve intake at meals. As of 2013, only 38% of hospitals reportedly have a room service program, though up to 43% of facilities say they were planning to incorporate this model (22). Room service increases a patient’s sense of autonomy in making decisions about their intake. Children with cancer often feel a lack of self-control and competence; and helping the child and the family learn to help themselves promotes self-esteem and compliance (23). MSK’s food service goes further by offering custom smoothies, milkshakes, and other calorically dense beverages and menu options that many patients find preferable to traditional oral nutrition supplements. A robust team with restaurant-trained chefs works to make culturally, ethnically, and religiously appropriate dishes when requested. On the Pediatric Patient Care Unit, the Executive Chef conducts weekly culinary rounds with the RDN for patients that may have longer length of stay or specific food preferences. For example, in the pediatric bone marrow transplant population that has a median length of stay of 21 days, patients often report menu fatigue to their dietitian. This led to the initiation of meal rounding and the need to create patient specific meals. For some patients the goal of care is to cook a meal that will bring a taste of home. In addition, the Cook Engagement Program, which is a new initiative to engage sous chefs and line cooks in patient care, brings more culinary expertise to the pediatric patient care unit to address such issues as menu fatigue, lack of oral intake, and symptom management. In conjunction with medical nutrition therapy, collaborating with the culinary and room service teams has made a difference in the way patients eat and think about food. Furthermore, the role of clinicians and culinarians intersect at the point where menus are created to meet therapeutic diet requirements. To improve patient experience, a variety of menus have been created that are nutrient specific, disease specific, culturally, ethnically, and religiously appropriate. Two of these focus on the dietary management of

### Table 2. BRATT I Diet (24, 25)

<table>
<thead>
<tr>
<th>Food Groups</th>
<th>Allowed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk and Dairy Products</td>
<td>Rice milk</td>
</tr>
<tr>
<td></td>
<td>Lactaid</td>
</tr>
<tr>
<td></td>
<td>Soy milk</td>
</tr>
<tr>
<td></td>
<td>Almond milk</td>
</tr>
<tr>
<td>Vegetables</td>
<td>Skinless baked, boiled, or mashed potatoes</td>
</tr>
<tr>
<td>Fruit and Juices</td>
<td>Banana</td>
</tr>
<tr>
<td></td>
<td>Applesauce</td>
</tr>
<tr>
<td></td>
<td>Diluted apple juice</td>
</tr>
<tr>
<td>Breads and Grains</td>
<td>Breads and products made with white flour</td>
</tr>
<tr>
<td></td>
<td>Dry toast</td>
</tr>
<tr>
<td></td>
<td>Rice Krispies, Rice Chex</td>
</tr>
<tr>
<td></td>
<td>Cream of Rice</td>
</tr>
<tr>
<td></td>
<td>White pasta</td>
</tr>
<tr>
<td></td>
<td>White rice</td>
</tr>
<tr>
<td></td>
<td>Rice porridge</td>
</tr>
<tr>
<td>Meats and Meat Substitutes</td>
<td>Boiled, scrambled, or poached egg whites</td>
</tr>
<tr>
<td></td>
<td>Eggbeater or egg white omelet</td>
</tr>
<tr>
<td></td>
<td>Creamy nut butters (1 tablespoon/day)</td>
</tr>
<tr>
<td>Fat</td>
<td>Use Sparingly:</td>
</tr>
<tr>
<td></td>
<td>Butter</td>
</tr>
<tr>
<td></td>
<td>Olive oil</td>
</tr>
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</table>
diarrhea often seen in patients who have had bone marrow transplants, abdominal radiation therapy, or some infectious diseases such as Clostridium difficile. Taking the principles of the standard bananas-rice-applesauce-toast-tea (BRATT) diet, the RDNs developed a two-step menu, BRATT I, Table 2, which is more restrictive in its menu options, and BRATT II, Table 3, which allows for more menu options as diarrhea begins to resolve.

The RDNs at MSK developed symptom and therapeutic diet specific recipes for patients to assist them with optimizing their nutrition status once at home. These can be found on the MSK website (https://www.mskcc.org/nutrition), allowing patients, caregivers, and even medical professionals to reference and prepare RDN approved recipes for specific conditions.

RDNs provide in-services to the room service staff and the medical teams frequently regarding these therapeutic diets and the indications for their use to ensure greater continuity of care. The RDNs also work closely with the patient unit Room Service Associate (RSA), who serve the meals, and can provide important updates regarding food preferences, dietary restrictions, and even new onset symptoms. The close collaboration between the clinical and room service team goes a long way in providing high quality care to patients.

Finally, MSK prides itself on offering pediatric patients even more than just autonomy in their food choices; it also offers them the opportunity to take part in a wide variety of food related events that provide a respite. Our Food and Nutrition Services Department has hosted events to teach children, caregivers, and families how to cook together, to make tasty and healthful foods that everyone will enjoy. A favorite event involves the delivery of a special breakfast of Green Eggs and Ham on Dr. Seuss Day. The role of the RDN is much further reaching than ever before. RDNs are empowered and supported to take the lead on clinical nutrition project and program development, leading to continued optimization of care. By utilizing the skill set of a dietitian in clinical and culinary areas of institutions, patient care can be significantly impacted in ways never before possible.

### Table 3. BRATT II Diet (24, 25)

<table>
<thead>
<tr>
<th>Food Groups</th>
<th>Allowed</th>
</tr>
</thead>
</table>
| Milk and Dairy Products | Rice milk  
Lactaid  
Soy milk  
Almond milk  
Soy Cheese  
Plain Yogurt |
| Vegetables   | Skinless baked, roasted, boiled, or mashed white and sweet potatoes  
Yucca  
Plantains  
Canned or very well-cooked vegetables without seeds, stems or skin (ie: green beans, squash, carrots, asparagus) |
| Fruit and Juices | Banana  
Applesauce  
Baked, peeled apples  
Canned soft fruit  
Melon (cantaloupe, honeydew, watermelon up to 1 cup/day)  
Diluted fruit juice (except prune) without pulp |
| Breads and Grains | Breads and products made with white flour (including flour tortillas, English muffins, bagels)  
Saltine, graham, and rice crackers  
White noodles and pasta  
Couscous  
Soft pretzel  
Cereal with less than 3 grams of fiber (ie: Rice Krispies, Rice Chex, Corn Flakes)  
Cream of Rice  
Oatmeal (not steel cut)  
White rice  
Rice porridge |
| Meats and Meat Substitutes | Grilled, Roasted, or Baked Chicken  
Roasted, sliced turkey  
Flaky fish  
Boiled, scrambled, or poached eggs, egg whites, or egg beaters (up to 2 whole eggs/day)  
Tofu  
Creamy nut butters |
| Fat           | Use sparingly:  
Vegetable or Olive Oil  
Butter Margarine  
Low-fat Mayonnaise |
| Beverages     | Pedialyte  
Decaffeinated Coffee and Tea  
Gatorade  
Crystal Lite  
Caffeine-free regular or diet soda in moderation (Ginger ale, 7-Up, Sprite, cola)  
Seltzer water  
Smoothies made with any of the “Allowed” foods |

### References


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**Contributors needed**

*Oncology Nutrition Connection* invites contributions from members on any of the following topics:

- Disease-specific overviews
- Book reviews
- Summary of a published peer-reviewed article important to oncology practitioners
- Case-study presentation
- Performance improvement or quality improvement projects
- Summary of a recent oncology nutrition conference proceeding
- Student/intern submissions on topics of interest to oncology dietitians

No writing experience? No problem. Mentoring is available for first-time authors. If interested, please contact the editorial team.

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Jennifer Lafferty: jennifer.lafferty@providence.org
A Multidisciplinary Approach to Survivorship

By Karen Berg, MS, RD, CDN

A cancer diagnosis can leave people feeling anxious, depressed, confused and alone. Research shows that support groups in this population help with many things including medical compliance and less feelings of depression (1). According to Katarina Miley, LMSW, oncology social worker at The Cancer Institute at St. Francis Hospital (The Cancer Institute) in East Hills, NY, “There are many research studies and publications that support the benefits of support groups in cancer patients.” Lisa Petgrave-Nelson, LMSW, OSW-C, oncology social worker at The Cancer Institute, agrees. “Support groups are especially important for cancer patients to attend with emotional support being the number one benefit,” she says. “Support groups give patients the opportunity to feel hopeful, exchange information, deal with the practical challenges of living with cancer and allow group members to share their experiences and emotions.”

As registered dietitians (RDs), we know the importance of good nutrition throughout the continuum of care for a cancer patient. People often turn to RDs after a cancer diagnosis because they want to know what to eat to improve their health and achieve better outcomes. Research has shown the benefits of a plant-based diet for cancer prevention and to prevent recurrence (2). Therefore, RDs at The Cancer Institute usually encourage patients to follow a plant-based diet.

At The Cancer Institute, monthly interdisciplinary meetings are held to identify how best to serve the patient population. The Cancer Institute patients are surveyed annually to find out what they are most interested in learning about or what programs they would like to participate in; and food and nutrition is always high on that list. In late 2017, attendance in traditional support groups was faltering and people were less likely to sign-up or attend support groups even if they did RSVP. In order to boost attendance at support groups, the dietitians and social workers tried a non-intimidating approach and it started out with the simple hypothesis: “If you bring food, people will come.”

RDs began to work with the St. Francis Foundation to apply for a grant for a collaborative series that included both nutrition education and social support. In 2018, with a generous donation by the Manhasset Women’s Coalition Against Breast
Cancer (MWCABC), *Nourish. Care. Connect.* was created. The three-week series took place in the main conference room at The Cancer Institute. Each week oncology dietitians lead a 30-minute food demonstration and tasting which was followed by meaningful conversation and activities led by oncology social workers. With funds provided by the MWCABC, RDs were able to purchase all food and equipment needed as well as cookbooks and other things participants were able to take home each week. RDs came up with the themes and menus and provided recipe cards of all foods prepared for everyone to take home.

Flyers (diagram 1) for the program were placed around The Cancer Institute and distributed to patients. Local partners and doctors distributed the flyer as well, and social media was also utilized to promote the event. People were asked to sign up in advance and report any food allergies, restrictions or intolerances that should be taken into consideration. Substitutions were always provided if someone who attended could not eat the main foods that were prepared. RDs wanted to use the series to bring people together over food so they took an all-inclusive approach so that everyone felt comfortable and could partake in the things being prepared. Fifteen people RSVP’d for Nourish. Care. Connect. in 2018 and there was an average of 10 patients and caregivers at each session, as opposed to 4-6 people on average for traditional support groups.

The theme in 2018 was easy, quick bites. The first week patients got to sample a red lentil soup (made in less than 20 minutes), the second week were energy bites that didn’t require any cooking (or food processors) and the third week was a secretly green smoothie and parfait bar. During one of the social worker-led discussions, participants were asked what kinds of things they do to make themselves happy. A long-time patient with metastatic breast cancer responded, “Programs like this... It’s nice to get out of bed and know I have something fun on my calendar and not just another doctor’s appointment.” Petgrave-Nelson was not surprised by this remark and affirms that “support groups contribute to the quality of life of the patients who attend.” Post-class surveys were given at the last session and all the feedback was positive.

On the surveys and throughout the series, many participants mentioned that they were curious about new gadgets and appliances that are supposed to make life easier, like the Instant Pot, Air Fryer and slow-cooker. When it was time to re-apply for 2019 grants, *Nourish. Care. Connect.* already had a following and a theme: “how to use new small appliances.” With all the patient enthusiasm, it got funded by MWCABC for a second time. The series took place in September 2019 with 16 people RSVP’d and an average of 12 attendees each week. The first week oncology RDs demonstrated how to make a high protein macaroni and cheese in the Instant Pot, the second week was several vegetarian snacks in the Air Fryer like crispy Brussels Sprouts, zucchini fries and...
onion rings, and the last week was a vegan chili in the Instant Pot.

A cancer survivor, who has several young kids at home, emailed the RDs the following week to report that all the recipes were accepted by her kids. “My pickiest child said the onion rings were good,” she wrote. “Almost as good as Burger King.” Her kids also loved the high-protein macaroni and cheese, which she said will now be a new staple in her home.

The foods prepared both years were predominantly plant-based and highly nutritious. The goal is always to introduce people to foods or recipes they have never tried before and really teach people that good food doesn’t have to be hard to prepare or taste bad. Throughout the program RDs highlight the healthy attributes of each food provided.

For the 2019 series social workers focused on self-care. “Self-care is essential for all of us but even more so for cancer patients who battle the physical pain, anxiety, depression, stress and every day worries,” said Petgrave-Nelson. “Whatever makes a patient feel good in a healthy way is considered self-care.” For the last session participants were given rocks to paint. One person wrote the word “breathe” on their rock as a reminder to be grateful for each breath. When social workers asked what patients are most grateful for, one patient with metastatic breast cancer, who came in holding two separate ice packs, responded, “Programs like this make me forget about all the pain I’m in.” Another patient who now has a recurrence of breast cancer that was originally diagnosed over ten years ago said: “This was my first ever cancer group event, I was encouraged to attend and I am very thankful that I did.”

Miley explains why this collaborative approach can be so successful. “Utilizing an interdisciplinary approach is important in working with any patient population, it is especially useful in working with patients who have cancer,” she says. “When a patient is diagnosed they are often working with many different individuals from a variety of disciplines, many of our patients wonder if all of these disciplines work together to provide the best care. Creating and being a part of interdisciplinary groups shows our patients that we are here and able to support them in many different ways.”

As an RD it is so important to teach people about good nutrition throughout the continuum of care, but in order for someone to even care about good nutrition they have to want to be involved in self-care. That’s where this kind of program is the perfect marriage. “I am so very grateful for these types of groups,” says another survivor. “They provide me with the support I need to get out of my house and not feel alone in dealing with my health issues.”

Food always brings people to the table, and good conversation is what keeps people sitting around long after the plates are cleared. If the program gets funded again in 2020 the hope is to do one-pot meals and sheet pan meals and to provide the attendees with recipes that are “easy”, “fool proof” and “have less clean-up.”

“Utilizing an interdisciplinary approach can help to increase patient trust in their team and see that their team has the ability to work together to bring them the best knowledge, content and experience possible,” says Miley. Food isn’t just for nutrition, according to Petgrave-Nelson. “Food is important for our physical and mental health. Whatever the recipe or dish, food helps to bring families together and promotes a sense of gratitude.” This social non-threatening environment provides a great platform to discuss nutrition and self-care, while increasing social interaction and building social support among cancer survivors.

References
You are invited to join us for a special 3-week series!

**NOURISH:** Enjoy samples of healthy, nutritious recipes made by our team of Dietitians. Learn how to use new appliances like an Instant Pot and Air Fryer!

**CARE:** Focus on self-care and taking time for yourself!

**CONNECT:** Come together with food and conversation!

**Wednesday, September 4th**
**Wednesday, September 11th**
**Wednesday, September 18th**

2-3 PM in Conference Room 122 (enter through Entrance E)

The Cancer Institute at St. Francis Hospital
2200 Northern Blvd, East Hills, NY

RSVP via phone 516-325-7506 or email stefani.pappas@chsli.org
Malnutrition Coding Denials: Documentation Matters

By Terese Scollard, MBA, RD, LD, FAND

Specific, precise and clear documentation surrounding medical and surgical diagnoses and treatments are critical elements of all professional medical documentation, including protein-calorie malnutrition (PCM). To avoid improper payments for unnecessary diagnoses and treatments, the Center for Medicare and Medicaid Services (CMS) creates requirements for payers, infrastructures and audit systems to ensure that hospitals comply with federal regulations. Some commercial payers also model these requirements. CMS requires documented evidence that supports patients’ diagnoses, and that treatments are specifically described, connected to the diagnosis, and accurate.

Clarity and consistency are sometimes elusive in the auditing and coding industry in general, and more specifically for our purpose, regarding PCM. There is juxtaposition for clinicians because federal auditors are paid based upon successful payment denials rather than accuracy from a clinical viewpoint.

Unfortunately, there is no clear standard that hospitals or health professionals can use to ensure they comply with documentation standards for PCM and many other diagnoses. There is also no standard between auditors, so different auditors can accept or deny the same patient’s PCM diagnosis for different reasons. This paper discusses the process, history, sources of confusion and disconnections in medical documentation and coding, and provides suggestions for improving specificity and clarity in documentation of the diagnosis of PCM, with the intent to help reduce coding denials. There is no guarantee these suggestions will reduce denials; however, the more specific, clear and precise PCM is described by the dietitian, physician, and other healthcare professionals, the less risk there may be to the hospital.

The Coding and Billing Process

Clinical documentation specialists (CDS) are employed by health systems to audit charts during the patient’s hospital stay to ensure there is adequate evidence to support the diagnoses before the patient is discharged.

The scope of practice of CDSs includes carefully phrased requests, also known as queries, to physicians for clarification of unclear documentation.

After discharge, medical coders apply codes using the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) coding classification system (1). In this system, called the Inpatient Prospective Payment System (IPPS), there are several diagnosis related groups (DRG) codes that label the severity of PCM using characterizations known as Complications or Comorbidities (CCs) and Major Complications or Comorbidities (MCCs) (1). When a CC or MCC is applied to the DRG, this may result in increased reimbursement to account for the increased costs of care associated with these conditions, including PCM. At the time of this writing, Mild and Moderate PCM are CCs, and Severe PCM is an MCC. In some cases, MCCs can result in a significantly higher amount of reimbursement to the hospital.

The Audit and Denial

CMS, being the source of reimbursement to hospitals caring for Medicare patients, wants to ensure that public money is spent appropriately and that improper coding does not occur. Therefore, the U.S. Department of Health and Human Services, Office of Inspector General (OIG) directs regional Recovery Audit Contractors (RACs) to audit medical records to identify improper payments and verify compliance with the DRG coding systems for Medicare billing. Payments may be deemed improper due to lack of evidence, such as inadequate documentation to support the diagnosis of severe PCM or the effect of PCM on patient care (2).

If RACs deem there is inadequate evidence, the original DRG code is reduced in severity level, or denied, and reimbursement to the hospital from Medicare is reduced. The RAC notifies the hospital that a different malnutrition code (moderate or mild), or no malnutrition code has been assigned instead of the original hospital-determined code that resulted in a higher severity level. This results in a coding change accompanied by instructions for the hospital to refund the difference in reimbursement to CMS, as RAC denials typically occur after the bill is paid by Medicare. The hospital may appeal the RAC denial within a specific timeframe with evidence that the denial should be reversed, but there is no guarantee the appeal will be successful (2).

This audit and denial process is not unique to malnutrition diagnoses; many diagnoses are audited because what is considered adequate documentation of evidence is debatable. The OIG also audits hospitals’ overall compliance with Medicare billing requirements for specific diagnoses, including PCM, in which they review a number of cases that are coded with a specific ICD-10 code (2). Examples of formal rebuttals for these detailed large volume audits from impacted hospitals can be found in references 3-5 and other OIG reports.

Erroneous Evidence Used in the Denial

It is important to understand any erroneous evidence used in denials in order to effectively refute it. Sometimes denials state that the adult patient was not severely malnourished because their body mass index (BMI) was not 16 or less. The reference given is a 1999 World
Health Organization (WHO) document, which instructs the reader on how to manage pediatric patients in refugee camps and during famines in developing nations (6). This 68-page document contains several sentences about adults, with a chart signifying that severe PCM only occurs at a BMI of 16 or less. This reference is inappropriate to apply to hospitalized adults in countries with well-developed healthcare systems, due to the dissimilar nature of the populations and settings. It also reflects a lack of knowledge related to obesity and PCM, as it conflicts with our current understanding of lean mass and survival in obese, ill patients (7-8).

Another reference frequently cited by RAC auditors is the Merck Manual which includes a chart listing BMI, serum albumin, total lymphocyte count, serum transferrin and delayed hypersensitivity as PCM criteria (9). This approach is not accurate or practical for clinical conditions, since PCM occurs at all BMIs, albumin reflects a stress response, and other measurements are typically not performed due to expense and lack of specificity to malnutrition (7-11).

Denials based on these criteria demonstrate that RACs may not understand the metabolism of albumin in disease-related PCM and/or are using a reference that should not be applied in clinical practice since more current evidence is available (12).

The Appeal Process
Coders conduct an initial review of the RAC denial to determine if the hospital should submit an appeal. Coders are not clinicians and cannot interpret clinical findings independently, thus they ask the dietitian, clinical nutrition manager (CNM), and/or a physician to review the patient’s medical record to determine if there was adequate documentation to support the diagnosis of PCM and demonstrate that it affected patient care.

A lead medical coder shares the details of the RAC denial statement, which often includes references, with the dietitian or physician reviewer. The reviewer will then study the medical record and locate details of nutrition care and evidence of PCM. The reviewer will seek documentation that describes the facility-approved malnutrition clinical characteristics such as the Academy/A.S.P.E.N. Consensus Characteristics (12) of PCM, and other pertinent data. Dietitians, physicians, nurses and other professionals’ notes will be reviewed for evidence of conditions, causes, and consequences connected to the patient’s PCM diagnosis. Nutrition specific documentation from all professionals caring for the patient should be reviewed; sometimes social work, nursing and rehab therapies refer to patient nutrition status indicators, nutrient intake, functional weakness, and family information that can also contribute to the body of evidence.

The clinical reviewer will then provide the coder with a written analysis of their findings, correct erroneous RAC interpretations and misperceptions, explain that references the RAC cited are not currently used in clinical practice or are not evidence based (if applicable), and the rationale for disagreement with the RAC denial. The dietician who reviewed the case typically does not write the formal response to the RAC. Instead, in their appeal letter, the coding manager, compliance officer, or facility legal authority incorporates the reviewer’s findings in their formal appeal. The coder will submit the appeal letter to CMS stating the facility’s disagreement with the denial, including the pertinent details provided by the reviewer, and may also provide organizational and clinical references, and policies and procedures to support the original diagnosis.

If the reviewer decides there is inadequate documented evidence, i.e., unclear, unspecific, vague, conflicting or absent documentation, they will respond in writing to the coder stating their agreement with the denial. The recommendation to the coder will be to not appeal the denial. The dietitian or CNM can then use this case as an example to teach nutrition and other healthcare staff about adequate documentation of PCM, to improve documentation policies, and/or to update the design or content of the electronic health record (EHR).

There are prescribed timelines and processes for facilities to formally respond to the denial and repay Medicare, or appeal the denial. CMS reviewers will consider the appeal, then agree or disagree and notify the facility within a specified timeframe. If CMS reviewers disagree (i.e. retain the original denial), there is a process for the facility to appeal the second denial should they so choose, as CMS has a formal, multilevel appeal process (13).

(Continued on next page)
Evidence to Use in the Appeal
The value the Academy/A.S.P.E.N. Consensus Characteristics (12) has brought to bedside clinical practice and to hospitals to ensure Medicare compliance cannot be dismissed or understated. Those hospitals with experience with RAC PCM denials, both before and after the 2012 Consensus was published, understand the significance, depth, value, and clarity that the Consensus brought by describing both the type and severity of PCM (10-12). While the Consensus is a paradigm shift, subject to change, based on expert opinion and in the process of validation, it has created a baseline for consistent, common interpretations and descriptions which can be applied in clinical practice (14-16). Other malnutrition criteria include those developed by the Global Leadership Initiative on Malnutrition (GLIM) (see sidebar).

Before the Consensus, the few hospitals with coding workflows for malnutrition typically used the commonly applied 1978 and 1997 characteristics for marasmus, kwashiorkor and a mixed type of PCM that are not currently relevant, practical or accurate (12,20,21). Some facilities collaborated with their medical staff to officially clarify that PCM occurs at any body mass index (12,22). Now the Consensus provides practical clinical information to contribute to the evidence supporting the nutrition and medical diagnoses of PCM to satisfy both clinical care needs, correct misinterpretations of albumin and PCM in obesity, and support clarity in documentation, and thus hopefully meet compliance requirements.

Organizational policies and procedures are key to a successful appeal. For example, medical staff and clinical nutrition policies that reflect the hospital’s malnutrition coding workflow and define PCM are useful. Medical staff approval of the Consensus authorizes workflow and define PCM are useful. Medical coding rules allow the medical staff to define facility practice in this manner (22). Additional references that can be supplied to the medical coder as evidence in the denial response include the 2012 Consensus, and articles describing the etiology based types of PCM (12,14,15), erroneous or outdated methods of diagnosing PCM (6,9), and PCM in obesity (7,8).

Dietitian Documentation
It is critical to remember that there are many other professions who review patient medical record documentation in addition to the bedside clinicians. Each reviewer has a role, and there are legal and financial implications by these reviewers and their interpretations of the strengths and weaknesses of nutrition documentation by the dietitian and other professionals. Downstream compliance and regulatory reviewers include CDSs, medical coders, commercial insurance reviewers, state, regional and federal auditors, facility compliance officers and others. Clinicians document for these other groups, not only for their bedside colleagues taking care of the patient.

To reduce risk of RAC audits, documentation of nutritional assessments and reassessment by the dietitian must be thorough, i.e., specific, clear and detailed. It is important to differentiate and specify the patient’s nutritional condition prior to admission and during the acute care admission. The dietitian must document the patient’s past and current nutrition status; all conditions and events that contributed to the nutrition diagnosis of PCM; the timeline, duration, severity and acuity of problems; care requirements and a treatment plan that targets nutritional gaps and addresses nutritional compromise and recovery. Specific suggestions to support adequate documentation are noted here.

Tips To Help Reduce Malnutrition Denials
• Clearly state the reason for the nutritional assessment or clinical evaluation, why the patient is being referred and treated, why any procedures are required, whether additional nursing time and close monitoring is necessary, and if the length of stay is impacted.
• Document all Consensus criteria that apply to the case when they are identified. A minimum of two is suggested to diagnose PCM, however it is recommended to document all conditions and any other nutrition-specific data that support the nutrition diagnosis.
• Clearly describe the reason a nutrition intervention is applied. The non-nutrition reviewer likely will not understand that a high protein milkshake is an intervention unless it is connected to the caloric or protein metabolic demand.
• Document and describe the location and appearance of specific body anatomy, palpate fat and muscle, and describe any suspected nutrition related lesions. Describe adequate and inadequate muscle mass, palpated muscle quality, and fat stores.
• Document the person’s ability to move and function, such as the ability to

GLIM is an attempt to align the international nutrition community with the World Health Organization to support improved clarity of the various types of malnutrition (17). BMI is included in the criteria, however it is emphasized that the use of BMI as a diagnostic measure for malnutrition is not appropriate in the US due to the disproportionate number of obese patients in this country. The Academy and A.S.P.E.N. have both stated that they intend to continue use of the 2012 Consensus characteristics, and a study validating the criteria is ongoing (18,19). The Academy/A.S.P.E.N. criteria fit well within the umbrella of GLIM; there is no restriction for documentation of GLIM criteria in addition to Academy/A.S.P.E.N criteria. In fact, practically speaking, clinicians have always documented low BMI and reduced muscle mass when it is pertinent to the case.
independently prepare and consume an adequate amount of food. Include measurements such as baseline and subsequent hand grip strength or other functional status conditions, and document any comments patients and others make of weakness or functional ability.

- Document details as to why fortified foods and supplements are needed.
  - Example: *Added high protein milkshake (15 gm protein) to increase protein intake to meet goal of 90 grams/day, to mitigate patient’s inability to eat adequate regular foods and to support healing of abdominal surgical incision.*

- Be clear and specific about the patient’s nutritional status and the target goals for calories, protein or other nutrients and fluids. It is considered best practice to state the target and gaps in both real numbers and percentages and the appropriate intervention (23). Describe the duration of the deficit, the resulting clinical problems, and the plan to reverse the deficit.

- State the reason the diet order, including texture or any other features, is being adjusted to improve intake or the ability to consume food independently.

- Rather than using the generic term, “malnutrition”, always state the severity (mild, moderate, severe) and etiology (chronic or acute illness, starvation) and always use the descriptive term “protein-calorie malnutrition”, such as in “Severe Chronic Protein-Calorie Malnutrition”.

- State the patient’s actual percent weight loss and actual intake change. Then compare to the Consensus ranges. The patient’s actual metrics are more specific than the cut-points in the Consensus. Comparison to the Consensus is useful, but document the patient’s actual metrics. Specify the weight lost prior to admission separately and that lost during the admission.
  - Example: *Weight loss 12 % (-22 lbs.) in 7 weeks prior to admission; 2% (-5 lbs.) since admission for a total of 14% (-27 lbs.) severe weight loss in 10 weeks.*

- Sometimes patients do not fall exactly into a stated timeframe category, and clinicians must use their best clinical judgement to assigning a severity level.
  - The term ‘significant’ can be used with the moderate weight loss percentages and timeframes. The term ‘severe’ can be used with the severe weight loss percentages and time frames.

- Conduct meetings, communications, and education about PCM with the CDSs in your facility. Encourage CDSs to refer cases to you during their chart reviews if they need clarity about documentation of nutrition problems. Encourage dietitians to contact CDSs if a physician is not responding to communications about the nutrition diagnosis or other concerns. CDSs can then contact the physician using their normal work process.

- Study professional journals and attend conferences to learn about PCM, nutrition-focused physical exam (NFPE), hand grip strength and national and international work related to PCM.

Even with clear, detailed documentation of two or more criteria, there are no guarantees that RAC denials will be prevented. Some denials may reference the Consensus criteria; however, the denial may state that two characteristics weren’t documented. For this reason, hospitals may require dietitians to document all Consensus characteristics that apply to ensure the inclusion of two or more criteria.

Sometimes RAC denials state two Consensus criteria weren’t documented, yet the reviewer finds that two or more criteria are actually present. This error can be detailed in the appeal. There have been discussions on list serves and in educational conferences on whether the recommendation for two criteria can be muscle mass and fat stores, or if grip strength and one other characteristic is sufficient. These or other combinations have not been tested with RAC, and CNMs therefore often recommend documenting all criteria that apply and any additional evidence pertinent to the patient’s nutrition status and treatments. Examples include BMI if pertinent, details of nutrition history, details of functional abilities, and observations such as ill-fitting clothing. The clinician should use clinical judgement within established guidelines and document all evidence related to the determination of the type and severity of PCM.

Health system professionals are often open to collaboration to improve documentation, especially medical coders and CDSs. Inter-professional educational programs are a step to ensure that clinicians, coders and CDSs are aligned in their understanding and interpretation of the types and severity of PCM and the impact of regulatory and compliance structures to their documentation practices. This learning and communication should help reduce RAC denials and federal audits. There are no guarantees, however. The ability to document, describe and justify your patients’ PCM diagnoses, the interventions applied and team interprofessional communication and care remain the best approach to avoid negative audits.

**Tips if You Receive a Denial**

- Ask the medical coders to send every malnutrition denial to you to review the case and provide information that can be used in the appeal and formal response to the RAC.

- Appeal and rebut, with organizational permission, the denial every time you believe it is erroneous, in collaboration with your compliance officers and medical coders.

- Provide evidence of your organizations’ actions to reduce the incidence of PCM, such as discharge meal programs, physician and administrative authorization for use of the Consensus criteria, meeting minutes, educational presentations to internal professionals and to the community, and data that is collected by the organization to improve care for the malnourished population.

- Demonstrate that your organization wants to know about the population so you can reduce PCM and provide better patient care. Do not let others presume you are only tracking PCM for reimbursement purposes.

- If a denied case is not well-documented by the dietician or has conflicting documentation from other healthcare providers, let your compliance officers know there is inadequate evidence to refute the denial, and use the record as a teaching tool and example of inadequate documentation of PCM.

(Continued on next page)
RACs may or may not have a healthcare background. Rebuttals should describe the findings such that non-healthcare readers will understand.

Include respected journal and textbook references.

Describe the significance of the current, modern understanding of PCM and how these conflict with historic and misapplied standards, such as the original characteristics from the 1970s and the 1999 WHO pediatric refugee standards. Describe any discrepancies or inconsistencies between current evidence and the references the auditor used to deny the case.

Persist with organizational and professional improvements to address PCM and share organizational policies and procedures, approved by appropriate leadership groups that reflect efforts at reducing and preventing PCM.

Find opportunities to teach other clinicians about malnutrition, and NFPE to increase their ability to diagnose, document and treat PCM.

Conclusion

The RAC may or may not use current nutrition references when they accept or reject the diagnosis of PCM. However, clear, detailed clinical documentation by the care team members, especially the physician and dietitians, remains the best way to prevent a coding denial. If a coding denial occurs, that same quality documentation is the best defense in an appeal.

References


18. GLIM Message to All A.S.P.E.N. and Academy Members, A.S.P.E.N. Clinical Practice Highlights, October 2018.


Disclaimer: This information is for educational purposes and should not be construed as legal or regulatory advice. Readers are encouraged to obtain advice and information from those with authority at their places of work.

Editor’s Note: We are highlighting select research posters presented at the American Institute for Cancer Research 2019 Research Conference, held in Chapel Hill, NC. Some of the researchers were eager to share their research and we present the implication of their research on the following pages.
Abstract

Although breast cancer (BC) is the 2nd leading cause of cancer death among US women [1]. Inflammatory Cytokines Link Obesity and Breast Cancer. Metabolic Syndrome. 2012;1:6. Overweight and obesity are known risk factors for BC. Inflammatory cytokines such as IL-6, IL-1β, and TNF-α are involved in the interaction of breast adipose tissue with breast cancer cells. 

Methods

Results

Conclusion and Future Studies

Acknowledgements

References

Figure 1. Study design. MCF-7 (ER+) and MDA-MB-231 (ER-) human breast cancer cells were treated directly with 100 uM EPA or BSA for 48h (A). MDA-MB-231 with human monolayer fat cells (HMFCE) were differentiated into adipocytes and treated with 100 uM EPA or BSA. Adipocyte conditioned medium (ACM) as well as cell-free ACM was collected and transferred to breast cancer cells for 48h. Changes in IL-6, NF-KB, STAT3, c-IAP-2, and FASN were evaluated by western blot. IL-6 was quantified by ELISA. Student’s t test was used to detect statistical significance at p<0.05.

Figure 2. Direct EPA effects (A) and CM-mediated EPA effects (B) on cell migration. MDA-MB-231 breast cancer cells were treated directly with 100 uM EPA or BSA for 48h (A). MDA-MB-231 cells were cultured with CM from murine or human adipocytes. MDA-MB-231 cells were exposed to CM from control, EPA-treated, or ACM-treated adipocytes for 48h. Direct EPA treatment for 24h reduced cell migration in both breast cancer cell lines as determined by decreased wound closure. CM obtained from murine in 24h or human in 48h reduced cell migration in both breast cancer cell lines as determined by decreased wound closure. CM obtained from murine or human adipocytes reduced cell migration in both breast cancer cell lines as determined by decreased wound closure.

Figure 3. ACM increased IL-6 secretion by MDA-MB-231 but not in MCF-7 cells. MDA-MB-231 cells were exposed to CM from murine, 3T3-L1 (A) and human, 3T3-L1 (B) adipocytes for 48h. IL-6 levels were determined in breast cancer cells by ELISA, using detection limit of 0.79 pg/ml (R&D Systems).

Figure 4. EPA effect on inflammation, fatty acid synthesis, and cell motility. MDA-MB-231 cells were exposed to 48h of EPA treatment and 48h 3T3-L1 adipocyte conditioned medium (ACM) with and without EPA pretreatment. CM was obtained from murine 3T3-L1 adipocytes after treatment with 100 uM EPA for 48h (A). IL-6, NF-KB, STAT3, c-IAP2, and FASN were measured. Next, cells were exposed to CM for 48h. IL-6, NF-KB, STAT3, c-IAP2, and FASN were measured. In addition, cells were harvested after 48h and proteins used for immuno-blotting. P<0.05 (N=3; Mean±SEM).

Figure 5. Effects of EPA pretreated 3T3-L1 adipocyte conditioned media on cell motility in breast cancer cells. Graphical representation of recovering MB-231 breast cancer cells after wound healing with and without 3T3-L1 ACM. EPA treatment. Representative wound healing images at 0, 4, 8, 12 and 24 h are presented (A,B,C). Statistical significance was determined by Student’s t test at p<0.05.

Figure 6. Figure 6. Effects of EPA pretreated 3T3-L1 adipocyte conditioned media on cell motility in breast cancer cells. Graphical representation of recovering MB-231 breast cancer cells after wound healing with and without 3T3-L1 ACM. EPA treatment. Representative wound healing images at 0, 4, 8, 12 and 24 h are presented (A,B,C). Statistical significance was determined by Student’s t test at p<0.05.
Feedback from lead author Fahmida Rasha, PhD Candidate in the Department of Nutritional Sciences at Texas Tech University

Please describe the type of research you and/or your laboratory are doing.

Our Nutrigenomics, Inflammation and Obesity Research (NIOR) lab, led by Dr. Naima Moustaid-Moussa focuses on understanding mechanisms linking adipose tissue endocrinology, expansion and inflammation to whole-body homeostasis. Emphasis is on the role of adipose tissue-derived bioactive hormones, metabolites and other substances that are secreted into the blood stream with the potential of affecting other distant body organs. NIOR lab uses cell culture, mice and model organisms (nematode C. elegans) as tools to understand mechanisms linking obesity to other chronic diseases, namely diabetes, cardiovascular disease, Alzheimer’s disease and breast cancer. Our NIOR lab has demonstrated that dietary bioactive compounds with potent anti-inflammatory or antioxidant effects (such as omega 3 fatty acids, tocotrienols and tart cherry anthocyanins) protect against metabolic dysfunctions in obesity, in part by reducing adipose tissue and systemic inflammation. Furthermore, we documented the role of adipocyte renin angiotensin system (RAS) in insulin resistance and inflammation. Specifically, overexpression of the angiotensinogen in adipose tissue increased glucose intolerance and inflammation.

Our lab also researched both the role of bioactive compounds, namely omega 3 fatty acids, and RAS in obesity-associated breast cancer. Dr. Arwa Aljawadi, former NIOR lab member and Fahmida Rasha, PhD Candidate, demonstrated that omega 3 fatty acids, namely eicosapentaenoic acid (EPA) reduced the negative effects of adipocytes on breast cancer cells. Moreover, Fahmida further demonstrated that RAS inhibition, using antihypertensive Angiotensin converting enzyme (ACE) inhibitor reduced adipocyte-induced breast cancer cell inflammation and migration. Fahmida used human adipocytes and breast cancer cell lines to identify individual and combined effects of inhibiting adipocyte RAS (using ACE inhibitors) and EPA on breast cancer cell inflammation and migration. This research has been recently expanded to a clinical retrospective pilot study in female patients with breast cancer to determine association between obesity, breast cancer, RAS and its inhibition. This research is in collaboration with NIOR member Dr. Latha Ramalingam, Research Assistant Professor; Dr. Rakhshanda Rahman, professor and breast cancer surgeon and director of at the Texas Tech University Health Science Centre (TTUHSC) Southwest Cancer Center; and Dr. Chanaka Kahathuduwa, Assistant Professor at TTUHSC Health Professions.

Future scope of this research?

In our present research we demonstrated that anti-inflammatory effects of omega 3 fatty acids in adipocytes may help reduce breast cancer cell inflammation and migration. Similar effects were found when combining omega 3 fatty acids (EPA) with an antihypertensive ACE inhibitor in vitro. Our goal is to further dissect the mechanistic basis for breast cancer cell and adipocyte cross talk, and how these dietary (EPA) and pharmacological (ACE inhibition) interventions exert their beneficial effects. Our next goal is to test these interventions against breast cancer progression using animal models of dietary or genetic obesity and breast cancer and possibly in other types of cancer. In parallel, we also aim to use breast cancer patient banked tissues and serum samples for large scale analyses that expand our exploratory pilot study to identify potential new biomarkers underlying associations among RAS, inflammation, obesity, and breast cancer. These may help better understand effects of obesity and RAS on breast cancer and identify potential clinical interventions to lessen these diseases.

Clinical applications of your research

Findings from our current and future research will aid to identify and establish mechanisms by which obesity-associated adipose tissue dysregulations contribute to breast cancer progression. This is especially important in women after menopause who are at a greater risk for breast cancer. Our studies will provide evidence-based information to design future dietary (fish oil) and pharmacological interventions by repurposing existing antihypertensive RAS inhibitors to prevent/treat obesity-mediated breast cancer.

Contact:
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Cancer-associated SF3B1 mutations create a therapeutic vulnerability to dietary serine restriction


The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University
Please describe the type of research you and/or your laboratory are doing.  
My laboratory is at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins. We are studying the biological and therapeutic implications of mutations in spliceosome genes in hematologic malignancies. In addition to the project on SF3B1 mutations and serine deprivation, we are studying how these mutations disrupt RNA splicing, energy metabolism (beyond just the serine synthesis pathway), and cellular differentiation. We also have several projects investigating new drug targets created by these mutations.

Clinical applications of this study  
Our study shows that cancers harboring mutations in the SF3B1 gene have an unusually strong need for an external source for the nonessential amino acid serine, in contrast to other cells, which can make their own serine inside the cell. As a result, dietary restriction of serine can, in mice, inhibit the growth of cancers with SF3B1 mutation. The clinical implications of this finding are that therapeutic strategies in human cancer patients could exploit this weakness of SF3B1-mutant cells by selectively depriving the cancers of serine. There are several ways to potentially do this, but one would be to perform a dietary intervention with a low protein diet that supplemented with purified amino acids except for serine, similar to the approach that is used in management of many inborn errors of metabolism. We are currently writing a pilot clinical protocol to test whether this could be feasible for patients with SF3B1-mutant myelodysplastic syndromes (MDS), and whether it could successfully lower serine levels.

Future scope of this research?  
As alluded to above, an important next step would be to test whether a dietary intervention could successfully, feasibly, and safely lower serine levels in human cancer patients. Also, important would be to further understand the mechanisms by which SF3B1 mutations create this vulnerability in cells, as this could improve the strategies to target it. Finally, we are beginning to investigate in the lab how serine deprivation might be optimally combined with existing therapies in oncology, since a dietary intervention would best be incorporated into oncology as part of already-successful treatment.

Was there anything that wasn’t mentioned in this abstract that would be worth noting?  
This dietary treatment approach specifically in SF3B1-mutant patients could be an example of a new strategy, a sort of “precision oncology diet,” where the dietary intervention would be matched to the particular mutations of the cancer, in the same way that tyrosine kinase inhibitor drugs are matched to mutations now.
Introduction

Several studies have shown notable effects in inhibiting proliferation and inducing apoptosis, mainly by anti-inflammatory actions. Nevertheless, there is still no evidence to support the use of OLE, as well as to study the mitochondrial properties of an Olive Leaf Extract (OLE) in breast cancer and human health. Nevertheless, at this moment, I would like to strengthen the use of a discarded part of plant, the leaves, which still remain a non-edible source rich in polyphenols that can play an interesting role in cancer. These polyphenols have been reported to interfere with initiation, promotion and progression of cancer by affecting tumorigenic cell transformation, particularly in mice xenografts (20) and in metastatic human breast cancer (21).

Results

The antiproliferative and proapoptotic effects of OLE were assayed in the MDA-MB-231 cell line. In Fig. 2, the cell viability of these cells treated with different concentrations of Olive extract (50-400 µg/mL) at 24 and 72h is reported. The dose-effect curve showed a 120% value of OLE need to 200 µg/mL, which lead us to set it as the best working concentration for all the following experiments. In Fig. 3A, we report the apoptosis profile obtained by FACs, with the same experimental conditions (100 µg/mL of OLE at 24 and 72h), confirmed by Annexin V/FITC analysis and by WB with the increased protein expression of apoptotic markers cleaved Caspase-3 and p27, as well as the overexpression of Cyclin E-specific of S phase at both 24 and 72h (Fig. 3B).

Additional experiments focused on the study of mitochondrial damage were performed by using confocal laser microscopy. In Fig. 3C, it is possible to observe a marked decrease in mitochondrial number and morphological changes in OLE treated MDA cells, which were evaluated by MitoTracker Orange probe. In Fig. 3D, instead the optical immunofluorescence images show an increased nuclear P53 phosphorylation upon treatment, suggesting the anti-proliferative effects of OLE.

Conclusion & Future Perspective

The experimental evaluation of the relationship of genetic background with diet, lifestyle and pollutants on cellular (in vitro) and animal models (in vivo) of breast and ovarian cancer, in order to better understand the initiation and progression phases of tumour linked to environmental stressors and food habits. Moreover, we intend to define the cellular mechanisms involved in the preventive tumorigenesis action of food components.

OLIVE LEAF AND DERIVED COMPOUNDS EFFECTS ON TRIPLE NEGATIVE BREAST CANCER MODEL

Reyes Benot Domínguez (1), Tupone MG (1), Catanesi M (1), Antonosante A (1), d’Angelo M (1), Benedetti E (1), Cimini A (1,2).

1. Department of Life, Health and Environmental Sciences; University of L’Aquila, Italy
2. Sbarro Institute for Cancer Research and Molecular Medicine and Center for Biotechnology; Temple University, PA

Feedback from lead author Reyes Benot Domínguez, Fellow in the Department of Life, Health and Environmental Sciences at the University of L’Aquila, Italy

Please describe the type of research you and/or your laboratory are doing.

The main objectives of my PhD project are the experimental evaluation of the relationship of genetic background with diet, lifestyle and pollutants on cellular (in vitro) and animal models (in vivo) of breast and ovarian cancer, in order to better understand the initiation and progression phases of tumour linked to environmental stressors and food habits. Moreover, we intend to define the cellular mechanisms involved in the preventive tumorigenesis action of food components.

Where is this research going? What are your ultimate goals?

The research takes place mainly at the University of L’Aquila in Professor Cimini’s laboratory (Department of Life, Health and Environmental Sciences, Laboratory of Neurobiology). Nevertheless, at this moment, I am at the Research & Development department of the pharmaceutical company Dompé Farmaceutici S.p.A and our aim is to find out the molecular pathways modulated by OLE, as well as to study the mitochondrial implications and changes due to the treatment in breast and ovarian cancer cells.

What are the clinical applications of your research?

We intend to demonstrate the antitumoral properties of an Olive Leaf Extract (OLE) in tumors of the reproductive system (Breast and Ovarian Cancer) in order to potentially reduce drug dosing and chemotherapeutic side effects, improve the treatment efficacy, increase life expectancy and the quality of life of patients in the Sanitary System. At the same time, we would like to strengthen the use of a discarded part of the Olea Europaea plant, the leaves, which presently still remain a non-edible source rich in polyphenols that can play an interesting role in cancer and human health.
Adherence to the WCRF/AICR Cancer Prevention Recommendations and colorectal cancer risk: underlying mechanisms in the healthy human colorectal mucosa

FC Malcomson, ND Willis, I McCallum, L Xie, DM Bradburn, NJ Belshaw, IT Johnson and JC Mathers. Human Nutrition Research Centre, Institute of Cellular Medicine, Newcastle University, UK.

1. INTRODUCTION

Colorectal Cancer

- Over half of colorectal cancer (CRC) cases are linked to lifestyle factors including diet and physical activity and are therefore preventable.
- Likely factors for which strong evidence exists linking them to CRC risk include:
  - The WCRF/AICR Cancer Prevention Recommendations include such lifestyle factors e.g. advise maintaining a healthy weight and limiting the intake of red and processed meat.
  - A 27% lower CRC risk was observed in EPIC Study participants with greater adherence to these recommendations (Luglio et al., 2015).
  - A 25% reduction in CRC risk per 1 point increment in adherence score has been reported elsewhere (McCallum et al., 2020).

Potential underlying mechanisms for effects of lifestyle on CRC risk

- The stage at which lifestyle factors affect CRC development is not well understood.
- The WNT signalling pathway regulates processes such as crypt cell proliferation and inflammation to maintain a healthy large bowel.
- Hyperactive WNT signalling occurs in ≥90% of sporadic CRCs.
- WNT pathway components are modulated by environmental factors e.g. dietary fibre intake, suggesting a potential mechanism for the effects of lifestyle on CRC risk.

2. METHODS

The DISC Study recruited 75 healthy participants from Wansbeck and North Tyneside General Hospitals, UK.

3. RESULTS

Table 1. Adherence scores for each Cancer Prevention Recommendation for DISC Study participants

<table>
<thead>
<tr>
<th>Cancer Prevention Recommendation</th>
<th>Score</th>
</tr>
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<tbody>
<tr>
<td>1. Be a healthy weight</td>
<td>0-1</td>
</tr>
<tr>
<td>2. Be physically active</td>
<td>0-1</td>
</tr>
<tr>
<td>3. Eat a varied diet in vegetables, legumes, nuts and beans</td>
<td>0-1</td>
</tr>
</tbody>
</table>
| 4. CONCLUSIONS

Greater total adherence scores and lower CHFCR concentrations were associated with lower expression of WNT signalling components, suggesting reduced WNT pathway activity, and improved markers of crypt cell proliferation. This study provides evidence for beneficial effects of adherence to the WCRF/AICR Cancer Prevention Recommendations on WNT pathway-related markers of CRC risk in the healthy human colorectal mucosa.

4. CONCLUSIONS

Feedback from lead author Fiona Malcomson, Human Nutrition Research Centre, Institute of Cellular Medicine, Newcastle University, UK

Please describe the type of research you and/or your laboratory are doing.
My research investigates relationships between lifestyle factors, such as diet, physical activity and obesity, and molecular markers of gut health and of colorectal cancer risk in the large intestine.

Where do you see this research going?
I hope that this research will lead to the identification of markers of gut health and of colorectal cancer risk that are modulated by dietary and other lifestyle factors. In addition, the findings could provide evidence for the underlying mechanisms in the large intestine behind the effects of lifestyle factors on colorectal cancer risk.

What do you think are some of the clinical applications for this research?
The identification of markers of gut health and colorectal cancer risk that are responsive to lifestyle factors, such as diet, could be used as endpoints in future studies and ultimately to identify those at greater risk of colorectal cancer who would benefit the most from cancer prevention strategies.

What further research do you think can be done to further back the conclusion you reached?
The findings from this research should be validated in another, larger cohort. Furthermore, relationships between adherence to the latest WCRF cancer prevention recommendations, published in 2018, and the measured outcomes will be investigated.
Ashwagandha: An Herbal Approach to Combat Cancer?

By Ranier Castillo, ACSM-CPT

Abstract

As lifespan increases, health continues to be highly emphasized. Longevity has put a spotlight on health due to the increasing prevalence of various illnesses such as cancer, compelling people to look for alternative therapies to maintain health. Ashwagandha (Withania somnifera) is an herb used in Ayurvedic medicine to combat various diseases such as cognitive decline and cardiovascular diseases. This review will examine the current studies published about the specific anti-cancer properties of ashwagandha and discuss practice implications if ashwagandha can be used in the field of oncology.

Introduction

In Western culture, natural approaches such as a healthy diet or herbal remedies are considered alternative or holistic medicine practices. Conventional medicine has been dominant in approaches to combat illnesses, especially cancer, without considering alternative medicine approaches to incorporate as possible tools to combat cancer. Herbal medicine, popular in Asia, continues to emerge as a topic of interest in Western countries as the cost of cancer treatments remain substantial. This review investigates the role of one such herb ashwagandha and its role in preventing and treating cancer.

Withania Somnifaria and its Biochemical Features

Ashwagandha (also known as Withania somnifera or “Indian Ginseng”) comes from the root of an evergreen shrub found in India (1) and along the east coast of Africa, the Middle East, and Northwestern Australia (2). It has been used for a millennia in traditional Ayurvedic medicine (3) and shows positive neurological health effects as it provides physical, physiological, and mental stress reduction (3,4,5). All parts of the herb (root, stem, fruit, and leaf) have shown to possess multiple benefits against other physiological disease and illnesses, such as infections, cognitive impairment, and anxiety (5).

Ashwagandha’s health benefits can be ascribed to three major groups of phytochemicals — terpenoids, alkaloids and phenolic compounds (5). Although all groups show positive benefits, the most significant and researched compound that contributes to therapeutic mechanisms of cancer is the terpenoid, withanolides (5,6). The anti-cancer compounds of withanolide are withaferin A, withanolide D, withalangolide A, withalangolide A, withalangolide B, withalangolide B-4,19,27-triacetate, withalangolide B-4,19-diacetate and withanone (5), and possess anti-tumor, antioxidant, and anti-inflammatory properties with withaferin A and withanone providing the most evident benefits (7).

Withaferin A

The first withanolide to be isolated and discovered is the steroid lactone, withaferin A (5). Through various animal studies, this compound has shown to target cancer cells and reduce the risk of tumor growth (5,6). Withaferin A prevents proliferative activation on leukemia cells by triggering the release of caspase -9, -3, -8, enzymes responsible for the signaling pathway to apoptosis (8,9,10). This compound isolated from ashwagandha also activates and preserves the tumor suppressor gene, p53 (1) and can suppress tumor expressing genes PLAU and Notch1, by DNA methylation and H3K4me3 demethylation (11). Szarc Vel Szic et al (12) determined a dose-response relationship between cancer cell viability and withaferin A dosage. Along with its apoptotic feature, this steroidal lactone has been shown to inhibit angiogenesis, with an IC50 value of 853.6 nano molars (nM) as the most sensitive dosage to withaferin A (12). Angiogenesis is a contributing factor for the growth of cancer cells and may lead to metastasizing cancer. However, withaferin A targets vimentin, an intermediate filament protein the cell responsible for angiogenesis and cancer cell growth (13), by causing vimentin fragmentation (8). Furthermore, it may inhibit genes, PLAU, CTSE, TGFα, ADAM8 and ITGα6, which are associated with chronic inflammation that can lead to metastasizing cancer cells (12).

Withaferin A also shows promising results when preventing and treating ultraviolet B radiation and benzoyl peroxide induced skin carcinoma (14). A possible explanation of these protective features is withaferin A’s capabilities to increase the antioxidant activity of superoxide dismutase, catalase, and glutathione peroxidase (2). These antioxidants play an important role in preventing oxidative damage to the DNA and other factors maintaining homeostasis. The most significant feature connected to withaferin A’s anti-cancer properties is the ability to reprogram MCF-7 and MDA-MB-231 cells, cell lines associated with breast cancer, and their oncogenes: JMJD3, JMJD2C, NCOA3 specific oncogenes (12). Further research is needed to determine what role withaferin A may play in the prevention and treatment of cancer.

Withanone

Withanone is another steroid lactone that has anti-tumor effects and can be found and extracted from the leaf of ashwagandha and has been referred to as i-Factor or i-Extract (1).
Survivin and mortalin, enzymes responsible for inhibiting caspase enzymes and p53, respectively, are inhibited when treated with withanone (15,16). Another inhibitory feature of withanone is how it interrupts the oncogenes, Aurora A and TPX2. Over expression of Aurora A is associated with various cancers, increasing the risk of breast cancer, colon cancer, and tumor growth (17,18). However, withanone interrupts the TPX2-Aurora A complex, which reduces the over expression of Aurora A (17). Although withanone is independently effective, the combination of withanone and withaferin A has shown a greater synergistic effect for the treatment of fibrosarcoma (HT1080) cells (1). The leaf extract, which includes withanone and withaferin A, suppresses p53 activity and exhibits tumor suppressing capabilities (1). If p53 becomes mutated, withanone and the other compounds from ashwagandha can reverse the mutated effects and reactivate p53 (1). When withanone’s dosage is increased with withaferin A (3:1 and 5:1 Withanone:Withaferin A ratio), normal cells may be targeted (19). Widodo et al (1) also observed high doses (0.1 nM per liter) of withaferin A causing toxicity to normal cells. Ideally, Gao et al (19) determined the best ratio to specifically target cancer cells with the use of withanone and withaferin A was a 20:1 ratio. Although there are implications that normal cells may be harmed, withanone has shown to also be protective to normal cells if exposed to toxic chemicals like methoxyacetic acid (20).

Discussion

Although, ashwagandha is used as a possible therapeutic treatment for various illnesses, efficacy in cancer is limited due to a few laboratory-based studies and lack of animal studies and large human clinical trials. Biswal et al (24) found potential improvements in cancer-related fatigue, but the survival rates results were inconclusive. This is possibly due to limited population size of fifty participants in the intervention arm and fifty participants in the control arm. Also, there has not been a consensus of optimal dose at which ashwagandha may treat cancer and its symptoms. Biswal et al (24) provided six grams a day, which may not have provided the optimal amount within their study.

Along with optimal dose, growth environment of ashwagandha may pose a challenge, since growth environment may impact the withanolide content. Widodo et al (1) found that ashwagandha grown in the laboratory may not contain certain withanolides found in naturally grown ashwagandha. This may provide limitations as majority of ashwagandha plants may not be feasible for cultivation in certain environments. It appears ashwagandha thrives in drier tropical and subtropical areas (2). In contrast, Kaul et al (25) found that hydroponic cultivation may be a solution for the limited geographical locations in which ashwagandha may prosper.

Although the current literature has shown some efficacy of ashwagandha in suppressing tumor expressing genes, inhibiting angiogenesis and enhancing antioxidant effect, reported toxicity to healthy cells and lack of animal and human studies makes it extremely difficult to make recommendations for its use in cancer patients at the present time. Ashwagandha is used for the prevention and management of some chronic conditions such as cognitive decline and cardiovascular diseases. However, ashwagandha cannot be recommended for the prevention or treatment of cancer at the present time. RDs should continue to educate themselves and stay abreast on emerging research on the role of ashwagandha in disease management.

References


22. Zhan T, Rindtorff N, Boutros M. Wnt signaling and treatment tolerance in patients (n = 78) with advanced nasopharyngeal carcinoma (NPC) undergoing chemoradiotherapy (CRT). Although participants lost weight with treatment, participants (n = 46) who received nutritional support at the beginning of CRT regained their weight, while the late group (n = 32) continued to lose weight. The late group received nutrition support only after the development of the side effects. Participants in the early nutrition support group also showed significantly lower rate of advanced mucositis, fewer days of treatment related toxicity and fewer unplanned hospitalizations (all p<0.05). The researchers concluded that early nutrition intervention is beneficial to patients with NPC, helping to maintain their nutritional status, enhancing treatment tolerance, reducing the hospitalization costs and improving participant’s quality of life.