# The Critical Role of Nutrition and Exercise: Optimization in the Patient With Cancer

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Presenter's disclosure of conflicts of interest is found at the end of this article.

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### Abstract

Undergoing surgery is one of the greatest physical and emotional challenges a patient can face, and doing so without preparation can lead to increased complications and mortality. At JADPRO Live Virtual 2021, Paul Wischmeyer, MD, EDIC, FCCM, FASPEN, emphasized the concepts of nutritional optimization and exercise optimization as being crucial and essential parts of all cancer care to optimize clinical and qualityof-life outcomes.

pproximately 2 out of 3 patients with gastrointestinal cancer are malnourished at the time of surgery, but only 1 out of 5 patients receives any preoperative nutrition intervention. According to Paul Wischmeyer, MD, EDIC, FCCM, FASPEN, Professor of Anesthesiology and Surgery, Associate Vice Chair of Clinical Research, and Director of Nutrition Support at Duke University School of Medicine, nutritional screening and optimization are essential prior to any major medical intervention.

During JADPRO Live Virtual 2021, Dr. Wischmeyer discussed nutrition screening and evaluation tools for nutrition, sarcopenia, and low muscle mass risk in cancer patients and shared evidence-based nutrition interventions to optimize before and after cancer-related treatments and surgery.

"No malnourished or unfit patient should ever have elective surgery or undergo bone marrow transplant or any major cancer therapy without nutritional and exercise optimization," said Dr. Wischmeyer.

# MALNUTRITION AND MUSCLE LOSS

As Dr. Wischmeyer reported, the prevalence of malnutrition in hospitalized adults is between 30% and 50% and declines further with prolonged hospital stay (Norman et al., 2008). By the time patients make it to surgery, approximately 65% are malnourished (Awad & Lobo, 2011).

This is important said, Dr. Wischmeyer, because malnutrition is directly associated with outcomes. One study of patients with lung or gastrointestinal cancer found that those who had weight loss or low muscle mass, diagnosed by CT scan at diagnosis, had a median overall survival of 8.4 months (Martin et al., 2013). Patients with normal muscle mass per CT scan, on the other hand, lived almost years longer on average. In addition, patients who are malnourished going into surgery have a 5-fold greater risk of mortality (Awad & Lobo, 2011).

Patients who have lost weight prior to major cancer surgery are also at far greater risk of complications. Even simple measures like albumin (a correlate of nutrition) can be an effective marker of risk before major procedures, said Dr. Wischmeyer. An analysis of more than two million patients in a large surgical database found that a low level of albumin was the fourth most predictive risk factor of death within 30 days of any major inpatient elective operation.

"Nutrition is the only modifiable risk factor that we can change for our patients in a week or two or three before surgery that can improve outcomes and reduce mortality," said Dr. Wischmeyer.

According to Dr. Wischmeyer, however, the "silent epidemic of malnutrition" that is complicating cancer and surgical care has failed to capture the attention that it deserves because patients tend to die outside of the hospital. "We're good at saving people and getting them out of the hospital, but most deaths from malnutrition happen after patients leave," he explained. "These patients will go to rehab or go to nursing homes and will die very shortly thereafter because of malnutrition, and many clinicians who work in the hospital don't see that."

"Malnutrition is an emergency for our patients in cancer and in cancer surgery, and it's something we really need to be better at intervening on and treating," he added.

# ENHANCED RECOVERY AFTER SURGERY PATHWAYS

According to Dr. Wischmeyer, many of the principles associated with enhanced recovery after surgery (ERAS) pathways are applicable to all cancer care, especially bone marrow transplants. As he explained, ERAS refers to patient-centered, evidence-based, multidisciplinary team developed pathways for a surgical specialty and facility culture to reduce the patient's surgical stress response, optimize their physiologic function, and facilitate recovery (Figure 1).

"ERAS programs are an incredible model for improving care," said Dr. Wischmeyer. "The main idea is to take patients who are not as fit or not as well-nourished as they could be and train them for surgery or for other cancer care like bone



**Figure 1.** What is ERAS? NPO = nothing by mouth; PONV = postoperative nausea and vomiting. Adapted from Ljungqvist et al. (2017).

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marrow transplant to improve their status prior to surgery."

Although there are several elements to ERAS pathways, Dr. Wischmeyer emphasized that nutrition is the key component—before, during, and after treatment. Nevertheless, a recent New York Hospital Association survey showed that 43% of patients at any given time in hospital in New York were NPO (nil per os). In other words, said Dr. Wischmeyer, they were being starved.

"If I were a prison warden and didn't feed half the prisoners, I'd get fired and probably end up in jail myself, but somehow it's okay for us to do this in very sick hospitalized patients who need the nutrition more than anyone," said Dr. Wischmeyer. "This really is an emergency, especially for cancer patients who have some of the highest rates of malnutrition and sarcopenia."

# **PRE-OP EVALUATION**

A joint consensus statement on nutrition screening and therapy published by the American Society for Enhanced Recovery and PeriOperative Quality Initiative (POQI) in 2018 emphasized the following recommendations (Wischmeyer et al., 2018):

- Nutrition screening is essential
- Protein is more important than calories
- Stop feeding late pre-op, restart early post-op
- · Oral nutrition supplements are needed for all
- Oral before enteral before parenteral
- Nutrition management is a team game

With respect to pre-op evaluation, Dr. Wischmeyer and colleagues at Duke University School of Medicine use peri-operative nutrition screen (PONS) questions for clinic-based nutrition screening. These questions include a body mass index (BMI) score (BMI < 18.5), a weight lost score (lost > 10 pounds of weight in last 3 months without trying), an intake score (eating less than 50% of your normal diet in the preceding week) and albumin levels (< 3.5). Answers to these questions are either drawn from the chart or acquired by phone screeners for all patients.

Because questions are subjective, Dr. Wischmeyer and colleagues suggest evaluation of lean body mass via CT scan when available to assist with nutritional risk prediction prior to surgery. They also use muscle-specific ultrasound with a device called MuscleSound to monitor nutrition delivery. "With muscle-specific ultrasound, we can measure muscle mass, muscle quality, and muscle glycogen in approximately 5 minutes," said Dr. Wischmeyer.

#### **PRE-OP INTERVENTION**

Patients with malignant factors are started on a high-protein oral nutrition supplement containing HMB ( $\beta$ -hydroxy- $\beta$ -methylbutyrate) for 4 weeks. Dr. Wischmeyer emphasized that reaching an overall protein intake goal is more important than total calorie intake in preoperative period, and the goal is more 1.2 grams of protein per kilogram of body weight per day.

"When you have a major stress like a surgery, the body breaks down muscle to generate amino acids to fuel the immune system and generate glucose," Dr. Wischmeyer explained. "You need the muscle mass to support this."

"One of the challenges we face as we age or get sick is anabolic resistance, which means it takes more grams of protein to make the same amount of muscle," he added. "Critically ill patients with cancer more severe anabolic resistance."

Dr. Wischmeyer noted that taking protein in boluses is a better stimulant for muscle growth and that high-protein drinks like Boost or Ensure before bedtime have been shown to improve surgical outcomes. A study of 800 gastric cancer patients with malnutrition prior to surgery who were randomized to 10 days of nutritional supplementation with nutrition drinks vs. no intervention demonstrated a 2.5-fold reduction in surgical site infections (Fukuda et al., 2015)

All patients, regardless of malnutrition risk, also receive immunonutrition (nutritional drinks that contain arginine) 7 days before surgery. As Dr. Wischmeyer explained, myeloid-derived suppressor cells associated with cancer deplete arginine levels, which suppresses the immune system. A study of more than 3,000 patients undergoing major surgery showed that, when given 5 to 7 days preoperatively, this simple nutritional supplement reduced the risk of infection by 40% and reduced the length of hospital stay by 2 days (Drover et al., 2011). Despite the effectiveness of this intervention, however, Dr. Wischmeyer reported that less than 1% of patients undergoing major surgery receive immunonutrition.

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# **POST-OP INTERVENTION**

Dr. Wischmeyer recommended that a high protein diet via diet and oral nutrition supplements be initiated on the day of surgery rather than NPO or just clear liquids.

"This is a big change for a lot of places, but it's a key part of enhanced recovery," he said.

A meta-analysis showed that patients who received protein-containing diets in the first day after surgery rather than NPO or clear liquids had a 70% reduction in mortality, a 61% reduction in surgical site infections, a 38% reduction in postoperative nausea and vomiting, and a 40% reduction in serious postoperative complications. Importantly, no adverse effects were attributable to early oral protein-containing diet (Pu et al., 2021).

"Patients do not aspirate more, and they don't break down their anastomoses," said Dr. Wischmeyer. "Sadly, most surgical patients, especially cancer patients, are NPO for more than 3 days after surgery on average (Franklin et al., 2011)."

"Surgery patients, especially GI surgery patients, are fed the poorest and are fed the latest, and these are patients at the greatest risk," he added.

Dr. Wischmeyer and colleagues recommend that all post-hospital patients after any major surgery receive a high-protein oral nutrition supplement in the hospital and after the hospital for at least 1 month. Just like in the pre-operative setting, Dr. Wischmeyer noted that reaching an overall protein intake goal is more important than total calorie intake in postop period. Post-operative protein intakes are also associated with reduced length of stay (Yeung et al., 2017).

"Just like before running a marathon, patients should carbo-load before all major surgery, and then receive post-op immunonutrition and a highprotein supplement," said Dr. Wischmeyer.

# EXERCISE

Exercise is another critical component of preparing for and recovering from surgery. In fact, recent data suggest that aerobic fitness is a more important indicator of health than BMI. A systematic review found that among "fit" older adults, all-cause mortality was the same, regardless of BMI (Yerrakalva et al., 2015).

"Just being obese or even being underweight does not increase your risk of all-cause death," said Dr. Wischmeyer. "On the other hand, being unfit, especially if you're obese or underweight, significantly increases your chances of death. Being unfit is more dangerous than being obese or even being underweight, which we used to think was the most detrimental thing."

Importantly, said Dr. Wischmeyer, it's never too late to get fit. Data have shown that there is a significant long-term survival advantage for patients who become fit later in life when compared with patients who never get fit (Blair et al., 1995).

According to Dr. Wischmeyer, cardiopulmonary exercise testing (CPET) is the future of exercise therapy to improve outcomes. Cardiopulmonary exercise testing can be done on a bike, a treadmill, or even in a hospital room with Bluetooth mask doing a step test. Regardless of how it's measured, lower exercise capacity before surgery is associated with increased risk of mortality and complications after major surgery.

"We can directly relate fitness to outcomes," said Dr. Wischmeyer.

An ongoing study at Duke called PReEVNT is looking to assess the clinical effectiveness of a 3-to-6-week prehab protocol involving highintensity interval training on a stationary bike combined with high protein oral nutrition supplements with HMB.

"We need to be addressing all the factors that lead to disability and complications in our patients, including malnutrition, the loss of anabolic hormones, and inactivity and physical dysfunction, and we have to bring that all together to optimize our patients," said Dr. Wischmeyer. "I dream of a day when our cancer patients and our surgery patients have the best opportunity to be prepared to run the marathon of their lives and have the best possible outcomes."

#### Disclosure

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