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19.1 Introduction

Non communicable diseases estimated to be cause for 63% of deaths, in India and cancer was one of the leading cause [1]. The number of patients with cancer in India is 1.3 million for the year 2020 (as calculated from hospital-based cancer registries) and the common 5 leading sites are breast, lung, mouth, cervix uteri, and tongue [1]. Prevalence of Malnutrition in Oncology (PreMiO) study identified nutritional impairment of 51% in patients coming for first medical oncology visit [2].

Timely identification of malnutrition in patients with malignancy is important as it helps in early intervention by nutrition supplementation which improves patient outcome. These patients usually present with classic signs of malnutrition like weight loss along with wasting of muscle and fat, leading to higher mortality and morbidity. So, if such patients get admitted to critical care unit, early initiation of feeding, increased nutritional needs to meet the higher goals and demands, complications of feeding should be taken care well to have best patient outcome and survival.

19.2 Goals of Nutrition in Malignancy

As malignancy itself a catabolic state, which is aggravated during an acute critical illness, goals of nutrition lies in identifying patients at risk or who have already developed malnutrition and optimizing nutrition with appropriate intervention, promoting early recovery and shorter hospitalization, improves survival, wound

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healing, muscle mass, immune function, gastrointestinal function, skeletal growth in children [3].

19.3 Effect of Nutrition on Clinical and Oncological Outcomes

Critical illness is associated with weight loss, cachexia, sarcopenia, increased catabolic response, stress due to changes in hormonal milieu and cytokine storm (systemic inflammation) following major physiological insults [4] which is exacerbated during malignancy. This increased metabolic response is followed by tissue healing phase. Both these phases lead to increased nutritional requirements. Malignancy per se is a hypermetabolic state that further increases nutritional requirements. So, early initiation of nutritional therapy (enteral preferred than parenteral) reduces harmful deleterious effects of patients hyperdynamic responses, reduces complications, decreases mortality and the length of stay [5].

19.4 Importance of Nutrition in Malignancy

The risk of malnutrition and its severity are affected by the tumor type, stage of disease and the antineoplastic therapy used [6]. Intensivist face various challenges in replacing nutrition in critical ill patient due to unstable hemodynamics, poor acceptance of feeds, malabsorption, communication gap, aspiration risk etc. [7]. Patients with malignancy adds to the above risk due to increased demands, loss of weight, massive bowel resection, perioperative nil per oral situation and nutritive needs are poorly understood.

Nutrition is an important factor in determining tolerance, morbidity and outcomes associated with specific treatment for malignancy [4]. Old age, chronic illness (inflammation), loss of appetite, nausea and vomiting, decreased oral intake, fatigue, chronic starvation & less care by relatives, utilization by cancer cells, chemotherapy & vomiting, coexisting illness are usually associated with malignancy. So, identification of those with preexisting malnutrition and persons at risk of developing it is crucial so that nutritional interventions can be implemented to prevent developing or worsening of malnutrition in high risk cases [4] artificial nutrition is indicated if patients are not able to take orally [8] Cancer cachexia [9] defined by ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment.

19.5 Definition and Risk Assessment Tools for Nutrition

As per ASPEN guidelines nutrition is defined as “An acute, subacute or chronic state of nutrition, in which a combination of varying degrees of overnutrition or undernutrition with or without inflammatory activity have led to a change in body composition and diminished function”.

Clinically nutritional risk can be assessed by acute weight loss, muscle bulk, skin thickness in posterior arm, BMI and lean body weight.

Various commonly used scoring systems that help in objective assessment of nutrition include

- Nutrition Risk Score (NRS 2002) [10], involves BMI, weight loss, dietary intake, and severity of illness scored from 0 to 3 with increasing severity
- NUTRIC Score [11], includes 6 variables -age, APACHE II, SOFA, comorbidities, IL 6 levels, days from hospital to ICU admission. High scores [6–9, 12] associated with worse clinical outcomes and low score (0–5) with low malnutrition risk

Some validated screening tools specific for oncological population [4], however less commonly used clinically:

- Malnutrition screening tool (MST), involving weight loss and change in appetite (both inpatients and outpatients)
- Malnutrition screening tool for cancer patients (MSTC), involves change in dietary intake, weight loss, performance status, BMI (only inpatients)
- Patient-Generated Subjective global assessment (PG-SGA) focusing weight, food intake, nutrition-related symptoms, function & activities
- Malnutrition Universal screening tool (MUST), includes BMI, unintentional weight loss >5%, reduced oral intake (only for inpatients).
- Mini Nutritional Assessment (MNA),
- Mini Nutritional Assessment—Short Form (MNA-SF)

None of the above scoring systems accurately assess patients the nutritional requirements [13], so nutritional requirements should always be individualized and patient specific nutritional plan is made.

Nutrition therapy: provision of either enteral nutrition (by enteral access device), and or parenteral nutrition (by central venous access).

Standard therapy: provision of intravenous fluids, no enteral or parenteral nutrition.

19.6 Components of Nutritional Therapy and Daily Requirements Calculation

Indirect calorimetry: The best method in determining energy needs in critically ill is Indirect calorimetry [14]. In its absence, weight-based equation of 25–30 kcal/kg/day used to determine energy requirements, 1.2–2 gm/kg/day for proteins can be used [15].

Resting energy expenditure(kcal/day) [16] = $((3.9 \times \text{VO}_2) + (1.1 \times \text{VCO}_2) - 61) \times 1440$.

Substrate requirement for a normal adult patient:

- Carbohydrates—70% of caloric requirements.
- Proteins—1–1.5 gm/kg/day.
- Lipids—30% of energy requirements.
- Fluids—30 ml/kg + replacement of abnormal losses.
- Vitamins and micronutrients if needed.
- Note: requirements should be individualized.

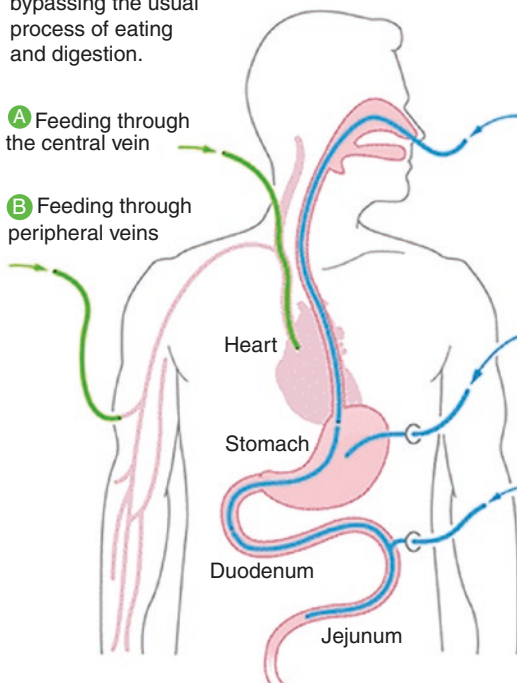
Parenteral and Enteral Nutrition

PARENTERAL NUTRITION

Feeding intravenously, bypassing the usual process of eating and digestion.

A Feeding through the central vein

B Feeding through peripheral veins



ENTERAL NUTRITION

Liquid supplemental nutrition is either taken by mouth or is given via a feeding tube.

Nasal or oral feeding tube terminates at, either:

C Stomach (Nasogastric)

D Duodenum (Nasoduodenal)

E Jejunum (Nasojejunal)

F Feeding tube that leads through an artificial external opening into the stomach (Gastrostomy)

G Feeding tube that leads through an artificial external opening into the small intestine (Jejunostomy)

Fig. 19.1 Various routes of nutritional therapy [17]

19.7 Routes of Administration (Fig. 19.1)

19.7.1 Enteral Nutrition

Nutrition therapy in the form of early enteral nutrition is the preferred form and should be initiated within 24–48 h in a critically ill patient unless contraindicated [18].

Providing nutrition via a tube, catheter, or stoma delivering nutrients to GI tract distal to oral cavity.

Advantages:

- More physiological,
- less invasive and less costly.
- lower hyperglycemia risk and blunt hyperdynamic response.
- improved nitrogen balance,
- improved wound healing,
- maintenance of gut integrity.
- Reduced infective complications specifically central line associated infections and pneumonia.

Disadvantages:

- Requires functional GI tract.
- Increased risk of gut related complication.
- May need more time to reach goal calories.
- Avoided in patients with hemodynamic instability requiring high vasopressor support/inadequately resuscitated, severe diarrhea, and enteral nutritional intolerance.

Complications:

- Pulmonary aspiration.
- Diarrhea.
- Hyper/hypoglycemia.
- Dyselectrolytemia.
- Hyperhydration.
- Dumping syndrome.
- Refeeding syndrome.

Even though high fat/low carbohydrate formulations reduce co₂ production, still it's not recommended as per recent study results.

Dosing of enteral nutrition-

- Energy needs: <http://www.surgicalcriticalcare.net/Guidelines/ICU%20nutrition%202017.pdf> – couldnt quote reference

- Normal adult: 25 kcal/kg/day.
- Cancer: Inactive, non ambulatory: 25–30.
Weight gain, nutritional repletion: 30–35.
Hypermetabolic, stressed: 35
- Protein needs:
 - Normal adult: 0.8–1.2 gm/kg/day.
 - Cancer: 1.2–2 gm/kg/day.

Composition of enteral nutrition:

- Caloric density: 1–2 kcal/L of feeding solution.
- Osmolality: 280–1100 mosm/kg H₂O.
- Protein: 35–40 gm/L of feeding solution.
- Lipids: long chain triglycerides derived from vegetable oil.
- Fiber content.

The enteral feed need to be modified as per need (Table 19.1).

Key points in enteral nutrition:

- Polymeric feeds (whole protein) and Soluble fiber are preferred
- Fluid restricted, calorically dense formulations considered in acute respiratory failure without hypernatremia
- No change in protein intake in case of AKI
- Periodic glucose monitoring in diabetic patients
- Standard enteral formulations should be used in acute and chronic liver disease

Tolerance of enteral nutrition should be monitored daily (passage of flatus, stool, absence of abdominal pain or abdominal distension), and avoid inappropriate cessation of enteral nutrition. Withhold enteral feeds in case of vomiting, abdominal

Table 19.1 Commercially prepared enteral feeds [19]

Polymeric feeds	Elemental feeds	Disease specific feeds
<ul style="list-style-type: none"> • Suitable for those with a normal or near normally functioning bowel. • Contain whole protein as the nitrogen source—Most provide 500 g/l of nitrogen and energy of 1 kcal/ml, • Commonly used commercial feeds are now clinically lactose and gluten-free and contain enough vitamins, trace elements, and essential fatty acids to prevent deficiencies. 	<ul style="list-style-type: none"> • Contain either pure amino acids or predigested protein and provide oligopeptides and amino acids. • Taste unpleasant and are relatively expensive, • Unless there is extensive impairment of gastrointestinal digestive and absorptive functions, they appear to offer little additional benefit. 	<ul style="list-style-type: none"> • Used in severely ill patients, such as those with multiple burns or trauma, respiratory failure, advanced cirrhosis, or acute renal failure. • Renal specific diets can be useful in chronic renal failure. • Little part in long term enteral nutrition.

Table 19.2 Gastrostomy versus nasogastric tube versus oral support

	Oral feeding	Nasogastric feeding	Gastrostomy
Duration of feeding	Longer	Shorter	Longer (>4 weeks)
Indications	Early stages of any systemic malignancies, no risk of aspiration	Any esophageal or head and neck malignancy with reduced mouth opening or difficulty in swallowing,	Esophageal stenosis, after esophageal resections
Advantages	More physiological Less risk of infection Less invasive	Less invasive compared to gastrostomy, easy to insert, useful in intubated patients	Useful in intubated patients, less risk of aspiration, less tube displacement
Disadvantages	Loss of taste, not possible in intubated patients, risk of aspiration if GCS poor	Tip of tube position to be confirmed every time after placement, prone for tube blockade, mucositis, ulceration, esophagitis or esophageal perforation	High cost [22], invasive technique, need special person for insertion, risk of infection Need trained care giver

distension, high NG output, high gastric residual volume, abdominal radiographs suggestive of obstruction.

Trophic feeding [20] (10–20 kcal/hr. or up to 500 kcal/day) can be tried in case of bowel intolerance instead of stopping enteral feeds completely.

Absolute contraindications for enteral feeds include intestinal perforation, ischemia and obstruction.

Gastric residual volume, not a part of routine care to monitor enteral nutrition (either for initiation or for stopping) [21]. In patients with high risk of aspiration—post pyloric enteral feeding, continuous infusion (preferred than intermittent boluses), head end elevation, prokinetic agents (metoclopramide or erythromycin) can be helpful in such situations. The feed can be given via oral cavity, nasogastric tube and gastrostomy. (Table 19.2).

Other modes of enteral nutrition include: nasogastric, naso jejunal, percutaneous endoscopic gastrostomy, percutaneous endoscopic jejunostomy, radiologically inserted gastrostomy, surgical gastrostomy/jejunostomy.

19.8 Parenteral Nutrition

Providing nutrition via central or peripheral intravenous access.

Indications:

- Short term: intractable vomiting,
 - non-compliant to enteral nutrition.
- Long term: inflammatory bowel resection,
 - radiation enteritis,

- chronic malabsorption.

Components: dextrose, amino acids (50% essential & 50% non-essential/semi essential amino acids), lipids, electrolytes, minerals and trace elements [23]. Composition varies with various preparation.

Complications: catheter related infections, carbohydrate related (hyperglycemia, fatty liver), lipid related (oxidation induced cell injury), GI complications (mucosal atrophy & acalculous cholecystitis), volume overload, and other metabolic complications.

Refeeding syndrome: can occur in both enteral and parenteral nutrition. Patients who had very little nutritional intake for >5 days are at risk of refeeding syndrome [23]. Metabolic derangements and clinical symptoms due to fluid shifts and electrolyte imbalance in already malnourished patient. Characterized by low phosphate, low magnesium, low potassium, low sodium deranged sugars and water imbalance. Can also be associated with respiratory, cardiac, and neuromuscular complications. NICE guidelines recommend commencing nutritional support at 50% of estimated energy requirements for 2 days in patients at risk of refeeding syndrome, thereafter increasing by 200–400 kcal every day [24] and close monitoring of electrolytes needed.

19.8.1 Assessment of Adequacy of Nutrition

Commonly assessed by *nutrition-related health indicators, nutritional intake, and energy expenditure* [25]. Nutrition-related health indicators include body mass index (BMI) and serum levels of albumin, prealbumin, hemoglobin, magnesium, and phosphorus. Serum albumin is most commonly used substance to assess protein nutritional status. Low levels of albumin reflects both nutritional status and prolonged physiological stress associated with the critical illness. Conversely, however, Gluck [26] found that albumin levels were not predictive of weaning success.

Nutritional adequacy [27] was defined as energy intake (kilocalories received on the basis of physician' orders) divided by energy required (determined by indirect calorimetry or physician orders).

Resting energy demand usually calculated by Harris-Benedict equation based on weight, height and age of the patient. But these formulas have unpredictable errors when used to estimate energy demand in individual subjects [28]. The recommended method of measurement of resting energy expenditure in critically ill patients is indirect calorimetry [28].

19.9 Role of Immunotherapy in Malignancy

Immunotherapy was assumed to be crucial in fighting against cancer [29]. Recent systematic review and meta-analysis demonstrated [30] immunonutrition to improve outcome in surgical patients in perioperative period, by reducing postoperative

infectious complications (moderate quality of evidence) and shortens the period of hospitalization (low quality) but does not reduce all-cause mortality. Formulas containing arginine and/or glutamine, ω -3 fatty acids, and ribonucleic acids modulate inflammatory and immune response in these patients [29]. Further research with larger patient samples and better study designs are still needed to give valuable conclusion.

19.10 Specific Concerns in Critically Ill Oncological Patients

19.10.1 Perioperative Period in Gastrointestinal and Head & Neck Malignancy

Patients with GI and head & neck malignancies are high risk of malnutrition because of dysphagia, odynophagia, reduced mouth opening, recurrent vomiting, malabsorption, loss of appetite, radiotherapy treatment like painful mucositis, altered taste, etc.

Enteral nutrition being first choice, feeding tube placement necessary prophylactically with inadequate oral intake [31]. Preoperative nutritional support in Head and Neck malignancy for 7 days decreases postoperative complications by approximately 10% in malnourished patients with weight loss of >10% [32].

In preoperative period, carbohydrate loading is safer, fasting can be limited to 6 h for solids and 2 h for liquids in patients without risk factors [33]. Early initiation of feeding recommended in postop period whenever possible [9].

Fluid and sodium intake need to be monitored in abdominal malignancies (causing peritoneal carcinomatosis), with obstruction or ascites, as excess sodium intake in such cases leads to fluid overload [8].

Hematopoietic stem cell transplant- There is high risk for malnutrition on HSCT treatment [34]. Immunonutrients did not show significant beneficial effects and therefore are not recommended for routine use. Neutropenic diets did not show a benefit over safe food handling approaches [34].

Feeding tube placement with thrombocytopenia(4)- thrombocytopenia(<1,50,000/ μ L) a common complication in critically ill patients with cancer either due to disease process or due to chemotherapy. It was earlier assumed invasive feeding tube access has the risk of increased bleeding tendencies. But few recent studies [35] concluded critically ill patients with cancer and thrombocytopenia are not at increased risk for bleeding complications after feeding tube placement than those without thrombocytopenia.

19.11 Other Special Conditions

- ARDS—trophic feeds in first week of hospitalization.

- AKI—standard ICU recommendations of protein 1.2–2 gm/kg and 25–30 kcal/kg/day followed (if receiving HD or CRRT increased protein up to maximum of 2.5 gm/kg/day).
- Hepatic failure—avoid restricting protein in liver failure, energy and supplementation based on dry weight rather than actual weight.
- Trauma—high protein polymeric diet preferably within 24–48 h of injury, immune modulating formulations (arginine) can be considered.
- TBI—early enteral feeding preferred
- Open abdomen—in absence of bowel injury, early enteral feeding preferred.
- Burns—protein of 1.5–2 gm/kg/day, early enteral feeding (4–6 h of injury).
- Severe sepsis—early enteral nutrition within 24–48 h of diagnosis, as soon as resuscitation complete and hemodynamically stable,
- Severe pancreatitis—enteral preferred over parenteral
- Hemodynamic instability—withhold till the patient is fully resuscitated, Can be continued with stable low dose vasopressors

19.12 Summary of Other Key Recommendations as per ASPEN Guidelines [18]

- Immune modulating enteral formulations should not be routinely used in medical ICU (can be considered in Surgical ICU patients)
- No recommendations for routine use of probiotic in ICU patients
- Antioxidant vitamins (C & E) and trace minerals (selenium, zinc, copper) not recommended routinely, but may improve outcome in burns, trauma, and critical illness with mechanical ventilation.
- Enteral or parenteral glutamine supplementation not recommended routinely
- In patients with low nutritional risk, exclusive parenteral nutrition can be withheld or delayed for first 7 days of ICU admission if early enteral nutrition not feasible or inability to maintain adequate oral intake in ICU
- In patients with high or low nutritional risk (enteral alone provides <60% of energy & protein requirements), supplemental parenteral nutrition considered after 7–10 days of ICU admission.
- In patients with high nutritional risk, exclusive parenteral nutrition initiated as soon as possible.

19.13 Conclusion

Malnutrition adversely affects outcome by increasing duration of mechanical ventilation, infection rates, gastric atrophy, growth reduction in children. Even though supplemental nutrition in critically ill patient with malignancy, may not reverse malnutrition, it may prevent progression and improve quality of life and survival.

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